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CONTENTS

Original Papers PAGE

Acromegaly in One of Uniovular Twins — AUBREY LEWIS 1
Psychoses associated with Pernicious Anaemia: With a Report of Two Cases — D. N. PARFITT 12
Traumatic Encephalopathy ('Punch Drunk') of Professional Pugilists — HARRY L. PARKER 20
Calcinm in Epilepsy — GWENVRON M. GRIFFITHS 29
Cholesterol Tumour (Craniopharyngioma) of the Pituitary Body — F. PARKES WEBER, C. WORSTER-DROUGHT and W. E. CARNEGIE DICKSON 39
The pH and Lactic Acid Content of the Cerebrospinal Fluid — L. HARRIS, E. WYN JONES and C. N. ALDRED 46
Colloid Cyst of the Tela Third Ventricle associated with Congenital Cystic Kidneys — E. WYN JONES and DOUGLAS H. COLLINS 53

Short Notes and Clinical Cases

Narcolepsy and the Machine Age; The Recent Increase in the Incidence of Narcolepsy — MAX LEVIN 60

Editorial

Changing Conceptions of Epilepsy 65
Abstracts 68
Reviews and Notices of Books 80

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THE JOURNAL OF NEUROLOGY AND PSYCHOPATHOLOGY

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Original Papers

ACROMEGALY IN ONE OF UNIOVULAR TWINS

By

AUBREY LEWIS,

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In the course of an investigation of twins a pair was discovered one of whom showed features of acromegaly while the other did not. They proved to be uniovular twins, and since they now differed so remarkably in stature and general configuration they were regarded as offering valuable and exceptionally rare material for the study of whatever hereditary factors may be concerned in acromegaly.

The twins, Frank and Albert W., are now 46 years old. Their personal histories will be given separately after a brief account of the family history.

Family History.—The family includes Scottish, English and Welsh members; on the mother's side there are many instances of unusually tall stature, none on the father's side.

The paternal grandfather was about 5 ft. 2 in. in height; the paternal grandmother died when the father of the twins was a baby and there is no relevant information about her. The two paternal aunts were both 'little mites' and the only paternal uncle was short and fat. The father of the twins was himself only 5 ft. 2 in. in height. He worked as a fish porter and was healthy for the greater part of his life; he died of a stroke at 65.

The maternal grandfather was a tall man, 6 ft. 1 or 2 in., of Scottish birth, and had two sisters who were tall and 'rawboned.' He was a healthy man, worked as a plumber and gas-fitter and died at the age of 50 through falling off a ladder. Concerning the maternal grandmother no information is available. The mother of the twins is now aged 79 and is still strong, energetic and in good health. She is a big woman, 5 ft. 10½ in. in height; there is no disproportion of features or skeleton. All her sisters are over 5 ft. 8 in. tall, and one of them has married into another tall family, the members of which together with the offspring of the union are shown in the appended pedigree (fig. 3). Her only brother was 6 ft. tall.

The members of the sibship in which the twins occurred are:—

1. Boy who died of fits when four months old.

2. George, age 54. Height, 5 ft. 7½ in. Has seven children, two of whom are similar twins ; none of his children is particularly tall.

3. Robert, age 52. Height, 5 ft. 7 in. Has two sons, of medium height, ages 19 and 17 years.

4. Harriet, age 50, rather short.

5. Emmeline, age 47, average height, married, healthy. Has four children of average height.

6. Frank, Albert } twins (see detailed accounts below).

7. Caroline, age 41. Height 5 ft. 2 in. Has five children of average height.

FIG. 1.—The twins at the age of 15.

8. Thomas, age 38. Height 5 ft. 5 in. No children.

9. Sidney, age 36. Height 6 ft. 2½ in. Has large hands and features (prominent jaw, long face, size 12 shoes).

Personal History of Albert W.—He was born nine minutes before his twin and was slightly longer and heavier. The delivery, like the pregnancy, was normal. There was only one afterbirth. It is not known whether instruments were used. He had a healthy childhood, except for measles and occasional bilious attacks. Like his twin he did well at school : they got the same marks and did well or badly in the same subjects. At the age of 18 Albert had grown into a very strong youth and became a grave-digger. After five years he was made foreman and has now for many years been general foreman of the graveyard, where he is still capable of exceptionally heavy manual work. His height has certainly not altered since the age of 27, but

in the opinion of his twin brother his face has grown longer in the last few years. There has, however, been no change in the size of his feet or hands or the circumference of his head for the last 20 years. At the age of 21 he ceased to need bigger shoes than the last pair he had worn ; he has had to have his shoes specially made (size 14). He thinks his head has altered in shape the last 10 years.

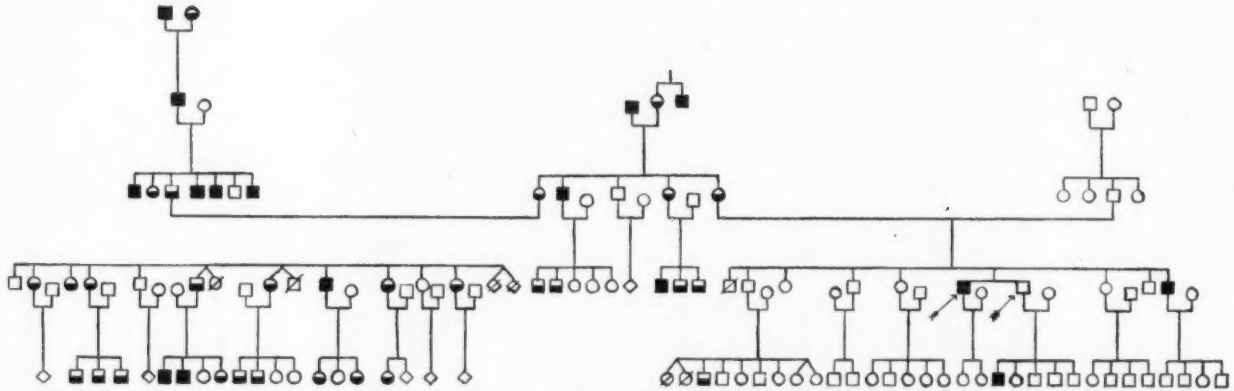
At the age of 17 or 18 he had trouble with his jaw locking. By the time he was 20 he had such a defective bite that he could not eat nuts or munch an apple ; at 23

FIG. 2.—The twins at the present time.

a dentist found great difficulty in fixing a denture and called attention to the defective development of his temporal muscles, for which he has since received treatment.

He married 23 years ago and has two daughters, ages 21 and 19, who are healthy and not above the average height. He has noticed no lessening of sexual desire in himself, and is potent.

His medical history has been rather uneventful. At the age of 12 he was swinging round a horizontal bar, 6 ft. high ; his hands gave way at the height of the swing and he fell on the concrete floor, hitting the back of his head. It bled a lot but he was not stunned ; he got up straightaway and went home but felt shaky. He returned to school that afternoon but stayed away for the next three or four days. He did



The symbols used are those recommended in the Eugenics Society pedigree schedule. ■ = 6 ft. or over. ◒ = 5 ft. 9 in., up to 6 ft.

FIG. 3.—Arrows indicate the twins.

not bleed from the nose or ear, and there were no ocular symptoms or headache subsequently.

Eight years ago he had an abscess in his axilla following a pustule on his finger, and was ill with it for seven months. For six years he has had acne rosacea, attributed by his doctor to digestive disturbances. He is not subject to headaches. He has always been very strong and boxed a good deal in his teens. He is an energetic, rather naive, good-natured man, proud of his height, strength and good health.

Personal History of Frank W.—His birth was normal, his childhood healthy, except for measles and occasional bilious attacks. He married at the age of 23, within two months of the date of his twin's marriage. He has four sons, the eldest of whom, age 21, is nearly 6 ft. tall. His health has been good; he was wounded in the wrist during the War. He is moderate in smoking and in drinking alcohol, but has a very big appetite. For many years he has run a window-cleaning business of his own. He is active, rather impatient, amiable and less naive than his brother Albert.

Points of Likeness and Disparity (as shown in history).—They were very alike during childhood. When they were in bed together their mother would have to turn them over to find a particular scar on Frank's head by which to identify him. They were continually being confused at school, and were usually distinguished by differences in their clothing, such as the number of buttons on the waistcoat. At the age of about 12 Albert's feet were larger than Frank's, but otherwise they took the same size clothing until the age of 14. At the age of 15 they were still so alike that one of them would pass for the other during a conversation of an hour or so with people who knew him well: Albert was, however, by this time, taller than Frank (fig. 1). He then shot up and by the age of 18½ was a very big fellow and continued growing, whereas Frank stopped growing at 17. Apart from accidents, they had during their earlier years the same illnesses and at the same time. Though not strikingly similar in personality, they have always got on very well together and tend to behave similarly in similar circumstances.

Physical Characteristics.—The difference in general appearance is striking. Albert is a giant, with a long face, narrow forehead, prominent superciliary ridges, very deep suprazygomatic hollows, wide-set broad cheekbones, thick lips, very large nose and chin, big hands and feet, thick fingers. Frank's stature and facial configuration can perhaps best be described as ordinary (fig. 2). Albert's bite is defective, the lower jaw being 1 in. in front of the upper when his mouth is closed. His palate is narrow and has a high arch. These features are not found in Frank.

The following measurements were made:—

	Albert	Frank
Anteroposterior diameter of head ...	20·9 cm.	19·3 cm.
Lateral diameter of head	14·8 cm.	14·2 cm.
Circumference of head 1 in. above bridge of nose	60·0 cm.	55·0 cm.
Chin to hair margin	22·4 cm.	19·3 cm.
Nose length	7·5 cm.	6·0 cm.
Nose breadth	5·4 cm.	3·6 cm.
Ear length	7·6 cm.	7·1 cm.
Transzygomatic	14·05 cm.	12·8 cm.
Length of upper arm	37·7 cm.	34·0 cm.
Length of forearm	29·2 cm.	26·5 cm.
Total length of lower extremity ...	94·4 cm.	80·2 cm.
Length of leg	46·2 cm.	42·0 cm.
Total height	(6 ft. 4½ in.) 194·3 cm.	(5 ft. 8 in.) 172·7 cm.
Total weight	16 st. 4 lb.	10 st. 7 lb.
Span	(84 in.) 213 cm.	

Colour of hair and eyes is the same in both. Albert's hair is thinner than Frank's. Albert takes size 14 in boots, Frank takes size 9.

The skull and hands of the twins have been X-rayed. In Albert there is much enlargement of the bones of the skull, of the typical acromegalic kind, with large air-sinuses and closed sutures; conspicuous prognathism; no definite alteration in the size and shape of the pituitary fossa. Frank's skull shows no abnormal features. In Albert's hands the bones are enlarged, unduly porous, with exostoses on the phalanges. This is not the case with Frank, in whom the appearances are normal.

Finger prints and palm prints supply evidence for uniovularity which may be regarded as conclusive.

DISCUSSION

The questions raised by this rare instance are (1) clinical, viz. the relation of acromegaly to the non-progressive acromegaloid forms; and (2) pathogenic, viz. (*a*) the constitutional factor in the development of acromegaloid conditions, and (*b*) the nature of the environmental factors which may provoke the morbid manifestations.

It may be taken for granted that acromegaly, acromegaloid conditions and gigantism are all referable to variations from the normal in the function and commonly also in the demonstrable structure of the anterior part of the pituitary gland. The second question is therefore one of the inherited and environmental causes of such changes in the pituitary.

The relation of acromegaly to gigantism, first discussed by Massalongo, Brissaud and Meige, Sternberg, and Launois and Roy, has become a more general problem of the relation of acromegaly, the progressive disorder, to other anomalies of growth attributable to changes in the function of the anterior lobe of pituitary and either not progressive or not permanent. Cushing [15] described a condition intermediate between acromegaly and gigantism. Ehrmann and Dinkin have given the name 'Acromegaloidism' to 'geringere, dauernde oder vorübergehende Steigerungen der inneren Sekretion des Vorderlappens der Hypophyse,' of which they report 40 cases. They divided it into familial acromegaloid types, in which the condition was permanent, and actual acromegaloidism, a more or less transient but more marked manifestation of symptoms, occurring at any period of life and approximating more closely than the familial type to true acromegaly in its clinical features. Bauer also has referred to these cases where after development has been completed the external signs of acromegaly are present without evidence of definite progressive disease; for this 'acromegaloid constitution' he is uncertain how far constitutional deviation in pituitary functions and how far autochthonous potentialities in the skeleton and other 'Erfolgsorgane' are responsible. Freudenthal gives a more complicated classification. There are now a great number of these cases on record, and it is certain that the patient Albert W. here described exhibits these acromegaloid characteristics rather than the familiar disease acromegaly. His strength, excellent health and retention of libido all point to this (for the sexual life, cf. Biedl). Many of the cases of acromegaly reported appear to have been examples of acromegaloidism or acromegaloid constitution. The difference is not at present one

that could be inferred from microscopical appearances in the pituitary gland of the affected persons: in both, hyperplasia of the anterior lobe, generally as eosinophilic adenoma, is found. Biedl thinks chromophobe cells may be responsible for transient acromegaloid changes, as in pregnancy. There is no reason to suppose that the clinical differences are of any fundamental type. Whereas there are strong grounds (occurrence of acromegaly in children) for questioning whether mere hyperfunction of the anterior pituitary can during the developmental period be held responsible for gigantism and acting during later life for acromegaly, it seems likely that the same disorder of function is responsible for acromegaly and acromegaloidism, the differences being conditioned by the degree and progress of the disorder of function, and perhaps also by the inherited constitution of the person affected.

The part played by inheritance in acromegaly is commonly overlooked, the question as to pathogenesis and ætiology being often disposed of by reference to the pituitary and other endocrine changes: but these have themselves to be accounted for. One might expect inherited factors to be significant here since there is so close an association between acromegaly (of which a fifth of the cases are giants) in one member of the family and tall stature in other members. A number of cases have also been reported of acromegaly occurring in more than one member of a family. The first report was a dubious instance of Fraentzel (1888), then Arnold (1891), Bonardi (1893), Schwoner (1897), and Cyon (1898) published cases; and in the present century 20 cases have been reported—by Bregmann (1900), Warda (1901), Fraenkel (1901), Schaeffer (1903), Franchini and Giglioli (1908), Cushing (1912, two cases), Allaria (1913), Sicard and Haguenau (1914), Lewa (1914), Oehme (1919), Machwitz (1920), Nobbe (1924), Möller (1924), Davidoff (1926, four cases), Müller (1930), Kienböck (1931). The papers of Banaudi and Strandell are not available to me in the original.

Of these cases, in four the patient's mother had also shown the disorder (Schwoner, Cushing, Allaria, Schaeffer); in four the patient's father (Bonardi, Kienböck, Fraenkel, Davidoff); in nine a brother or sister (Cyon, Möller, Müller, Oehme, Sicard and Haguenau, Nobbe, Bregmann, Fraenkel, Davidoff); in four a son or daughter (Fraentzel, Machwitz, Warda, Franchini and Giglioli); and in three a collateral (Lewa, Davidoff). In three instances more than one of the patient's relatives was affected (Oehme, Fraenkel, Nobbe). Unfortunately data permitting accurate diagnosis are often not available concerning the affected relative; in some cases the diagnosis is disputed (thus Marie considered the daughter of Fraentzel's case to have shown hypertrophic pulmonary osteoarthropathy, not acromegaly), and for the patient himself it is often difficult to be sure. Thus Lewa's two cousins (in whose family there was much consanguinity) showed changes in the soft parts without skeletal changes, but in one of them the diagnosis was supported by the discovery of an eosinophil adenoma of the pituitary gland. In Arnold's case (which was the subject of a stormy controversy between

Friedreich, Marie, Erb and others), as in those of Müller, Oehme, Kienböck, Sicard and Haguenau, Allaria, Warda, Bregmann, and Fraentzel, the changes in the affected relative were circumscribed and anomalous, suggestive of macrosomia; Müller would regard his own case as well as Arnold's and Oehme's as representing a special hereditary disorder. Apart from these somewhat doubtful examples one finds cases where the patient is acromegaloid, e.g. Cushing's kyphotic man, whom he described as intermediate between acromegaly and gigantism, or Nobbe's woman of 40, though the majority of the patients themselves are typical examples of slowly progressive acromegaly. Among the relatives, however, only a few showed definite acromegaly, e.g. the cases of Schwoner, Machwitz, Schaeffer; in many the diagnosis is doubtful since one is dependent on hearsay, photographs, etc.; in other the condition was probably an acromegaloid one (Bonardi, Nobbe, Fraenkel). In four of the families other relatives were unusually tall (Schwoner, Cushing—both cases, and Nobbe). In three cases the pituitary disorder was associated with other endocrine anomaly in the same person (thyroid disorder in Möller's cases, diabetes mellitus in that of Schaeffer and Machwitz). Several instances, like those of Parhon and Cernantzeano, Étienne and Richard, may be found in the literature describing a patient with acromegaly who had a relative with hypopituitary features: a third brother in Cyon's sibship had pronounced symptoms of this kind. Such cases have been omitted from the series here collected, which is concerned only with the occurrence of acromegaly or acromegaloid features in several members of one family.

Reviewing these cases it will be seen that in the relatively large literature of acromegaly very few examples of a familial incidence have been reported (cf. Falta). Among these anomalous forms have predominated; in the same family definite acromegaly of early or late onset, acromegaloid features of a mildly progressive or stationary kind, or partial enlargements of the extremities may be found. It would appear that the hereditary factor is for the most part unimportant in acromegaly but that in some families there is an inherited predisposition to pituitary anomalies in the direction of perverted or overactive function of the anterior part; this predisposition only becomes manifest in certain rare circumstances, and the modes of its manifestation are variable. This agrees with the views of Bauer. The conditions for its manifestation are most commonly satisfied in ordinary tallness hardly amounting to gigantism, most rarely satisfied in severe progressive acromegaly.

In so far as the patients reported in this paper are unquestionably uniovular twins, their hereditary equipment may be assumed to be identical or almost identical. Since one of them, Albert, is an acromegaloid giant and the other not, it may be assumed that environmental conditions have been present which favoured the manifestation in Albert of his predisposition to a pituitary anomaly. That such predisposition was present in both of the twins is probable when one considers the large number of antecedents and collaterals

of unusually tall stature and the fact that the twin of normal height (5 ft. 8 in.) has a son who is 5 ft. 11 in. high at the age of 20.

What then are the environmental factors which have favoured the acromegaloid manifestations in one of these twins? The brothers were almost identical in appearance and size until the age of 14: then Albert began to grow faster and was soon noticeably taller, bigger and stronger than Frank. It may therefore be assumed that any environmental factor responsible for Albert's more rapid growth had been operative before this. The only circumstances that one can regard as significant in this connexion, with one's knowledge of the patients' histories, is the accident which Albert had at the age of 12. The significance of cranial trauma in the ætiology of acromegaly is usually thought to be very slight. Bassoe denies it any. Cushing reports no instance of it, though in six of his cases of hypopituitarism there was a history of cranial trauma; Davidoff reports two cases out of a series of a hundred acromegalics; Bauer says that physical trauma seldom plays a part in the ætiology of any endocrine disorder. There are, however, two striking cases in the literature. Nobbe reports a man who shot himself in the head at the age of 16, causing fracture of the base of the skull, followed by polydipsia, polyuria and loss of libido, and later by rapid and excessive growth of the long bones, with prognathism and enlargement of the nose, lips and tongue. A radiograph taken at the age of 23 showed a bullet in the sella turcica; there were also X-ray evidences of acromegalic changes in the bones. Bleibtreu reports a less striking but still more relevant case. A boy of 16 fell downstairs and hit his head, but the injury was regarded as trivial and he did not have to lie up after it. Next year he was observed to be growing very rapidly and by the age of 21 his height was 196 cm. (6 ft. 5 in.); his superciliary ridges, nose and lips were thick and prominent. At autopsy, following his death from tuberculosis, the sella turcica was found filled with a mass of golden pigmented fibrous material in which pituitary alveoli were seen on microscopical examination. It is not certain that the trifling injury recorded in this early case was responsible for the hæmorrhage into the pituitary with subsequent changes, leading to the appearance of acromegaloid features, but there was no other explanation forthcoming for the lesion found: and if it be accepted, it may be regarded as furnishing support, however slender, for the view that cranial trauma played a similar part in the genesis of Albert W.'s acromegaloid condition.

The final point of interest in this case lies in the object-lesson which it provides that very close similarity of adult twins as to appearance and measurement must not be taken as the only or essential criterion of uniovularity. It might be most misleading, as in this case. (The earlier history, also finger and palm prints, put the uniovularity here beyond dispute.) Minor variations in uniovular twins have been recorded. Weitz has found deviations in body weight and size of skull of uniovular twins but none as great as in this pair. There is no other case of acromegaly in indisputable uniovular

twins on record. Allaria's doubtful case (a child of 21 months) was a twin, but there is no information in the report as to points of likeness or dissimilarity except that one of the twins was healthy and the other had macrodactyly. Möller describes two brothers, twins, who showed ichthyosis shortly after birth and ever since ; one of them at 16 began to grow rapidly, especially as to the extremities and nose, and also had pains in the head, dizziness, tiredness and mental retardation. He is now 158·5 cm. high and has large hands and feet, lips and tongue. The other twin has shown marked enlargement of the nose, but no enlargement of the hands and feet, and no headaches, tiredness or retardation. His height is 162 cm. The author regards the condition as a pluriglandular syndrome in which thyroid and pituitary are chiefly concerned. He does not give sufficient information to enable one to decide whether the twins were uniovular ; in a photograph they look very alike. Siemens has reported many cases of thyroid disorder in uniovular twins without divergence, but there is an interesting communication by Borchardt showing the influence of exogenous factors working through the endocrine glands. It is, however, a rare conjunction that could result in so dramatic and instructive a divergence between so-called identical twins as that reported here.

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PSYCHOSES ASSOCIATED WITH PERNICIOUS ANÆMIA

WITH A REPORT OF TWO CASES

By

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The terminal stages of pernicious anæmia are frequently complicated by mental fatigue and enfeeblement, by drowsiness and apathy and by mild depression or delirium, symptoms which are common to the terminal stages of several other disorders, while even in earlier stages of the disease the combination of a measure of apathy and mental depression is said by Vaughan [1] to be so usual that a sudden improvement in the mental outlook is as characteristic and as important a sign in pernicious anæmia of satisfactory response to liver as is a rise in the reticulocyte count. Again, it is an obvious possibility that pernicious anæmia may coincide with any type of psychosis, developing before or after the onset of the mental disorder, and it can be expected that the onset of so severe an illness would occasionally precipitate an incipient mental breakdown.

The combination of anæmia and psychosis is more frequent than can be always accounted for by mere chance, but the ætiological relationship of the anæmia to the psychosis is not easily settled.

The actual incidence of psychotic changes in pernicious anæmia is widely estimated by different observers, probably on account of the individual differences of opinion as to what constitutes a psychosis. Thus Cannon and Hayes [2] in a recent textbook of psychiatry state that 5 per cent. of patients with pernicious anæmia develop distinct mental changes, while Läufer [3] found only one case of insanity in 190 cases of this anæmia, and he quotes various authorities who have found the incidence even less than this. The differences in individual conceptions of psychotic changes become plain when the symptoms described as occurring are reviewed. Apathy is recorded by Richardson,[4] Woltmann,[5] Naegeli [6] and Piney,[7] the last-named stressing the association of this with incooperativeness. Alterations of character were noticed by Naegeli,[8] Hulett [9] and Émile-Weil and Cahen,[10] and abnormal irritability by Naegeli [6] and by Bremer.[11] Langdon [12] described an apprehensive neurosis appearing as a manifestation of pernicious anæmia; Barrett [13] and Phillips [14] believe that paranoid states are common. Depressive states, varying from simple retardation to profound melancholia, are agreed to be common by most writers, while Émile-Weil and Cahen have observed states of excitement. The remaining descriptions of psychotic manifestations

occurring with pernicious anæmia can be considered as variations of a confusional state, akin to a toxic exhaustive psychosis, with confusion, agitation and restlessness and a tendency to delirium and unpleasant hallucinations at night. Such states are described by Läufer, Naegeli, Émile-Weil and Cahen and others. The mental symptoms observed can be summed up roughly as those of delusional states, of depressive or manic states or of toxic confusional states, if one excludes irritability, apathy, mild depression and character changes which would be inevitable in a certain proportion of sufferers from pernicious anæmia. These symptoms have been most frequently found with fully developed anæmia, particularly in the terminal stages, but Mathieu [15] states that mental symptoms may occur at any stage of the anæmia, while Piney and Phillips have described symptoms commencing after the institution of liver treatment, though most agree with Émile-Weil and Cahen that mental symptoms are rare when the blood is normal.

The pathological factors underlying the appearance of psychotic symptoms have been the subject of divergent views. An original psychopathic disposition is stressed by many ; thus Naegeli thinks that an abnormal constitutional ' make-up ' is the chief cause ; Schaumann and Saltzmann [16] think that the psychosis develops in a hereditarily tainted disposition and Phillips that symptoms occur in the predisposed ; Hackfield [17] believes that such psychoses are due to environmental traumata. Schneider [18] divides his cases into two groups, the first where the anæmia lights up an endogenous psychosis and the second where the psychosis is symptomatic of a severe anæmia. Taterka and Goldmann [19] correlate the mental state with the anæmia and describe a case where the mental symptoms grew worse during the initial fall of hæmoglobin following liver therapy, to improve steadily as the hæmoglobin increased. Atkin [20] found psychogenic factors, but considered the anæmia the chief cause, whereas Warburg and Jorgensen [21] described six cases of psychosis with megalocytosis and anacidity, but without anæmia, which improved on liver treatment ; Hackfield found no parallelism between the condition of the blood and the state of the psyche.

The theory that toxins are generated by the disturbed metabolism consequent on the anæmia is upheld by Schaumann and Saltzmann, and by Landelüdecke,[22] who quotes a case with no cure of the psychosis on improvement in the anæmia, a fact which he explains by assuming that prolonged toxic action had destroyed neurones. Hackfield negatives the toxin theory, since so few patients with pernicious anæmia develop mental disorders and since neurological symptoms so seldom recover. It seems clear, as Hackfield states, that pernicious anæmia does not cause a psychosis in the way that syphilis causes general paralysis. The consensus of opinion favours the view of an original psychic weakness which may be augmented by environmental difficulties, giving way under the physical strain imposed by pernicious anæmia. The part played by anæmia or toxæmia or both is probably greatest in the toxic-exhaustive type of psychosis. The diminution of hæmoglobin

in the blood is probably not so important in this respect as the measure of toxæmia, although Barcroft [23] has shown that anoxæmia can produce confusion, lethargy and irritability. The nature of the toxins concerned cannot be known until it is settled whether pernicious anæmia and the spinal cord changes are due solely to the absence of the intrinsic factor of Castle,[24] or whether toxins are subsequently absorbed or generated.

Important as predisposition undoubtedly is, it is clear from the evidence available that the successful treatment of the anæmia usually leads to a complete cure of the psychosis, but neurological signs, as in pernicious anæmia without psychosis, are slow to improve, if they improve at all. Hackfield insists that liver treatment does not help the psychosis and that it must be separately treated, but, as a rule, with the anæmia cured, the mildest form of persuasion and encouragement is sufficient to enable the patient to overcome his own psychological difficulties. Hackfield warns against the risk of suicide in depressed cases, and recommends insulin and glucose therapy for malnutrition and thyroid extract if the basal metabolic rate is low, but these are side-issues in treatment, to be considered in individual cases.

PERSONAL CASES

The first of the following two cases presents several features of interest and is one of the chief reasons for this communication.

Case I.—E. C., female, age 33.

Of her parents, the mother died young and left the father with six daughters, the patient being the youngest. One by one the other daughters married and finally she was left alone with her ageing father. He was a blacksmith, but age was sapping his strength and the patient had to do a great deal of his heaviest work for him, duties which came easily to her, for she was a very strong, active and adventurous girl, an excellent hockey player and swimmer, with a weakness for gambling. Life with her father was not a happy one and she hoped to escape by marriage as her sisters had done, but this prospect became increasingly less certain as the years passed. At 30 she was a disillusioned woman, resenting the comparative freedom of her sisters, tired of the drudgery imposed by house duties and the additional work in her father's failing business, and finding the greatest difficulty in suppressing the anger and distaste she frequently felt for her father, now a querulous old man approaching 80. Thereafter she became progressively more lazy and slovenly and indulged her craving for gambling with every penny she could obtain, never, however, complaining to her sisters or showing the antipathy she felt towards her father. Following the development of extreme inertia with marked depression and delusions of unworthiness, she was certified and admitted to hospital on April 10, 1932.

On admission she was depressed, apathetic, retarded and mildly confused, with ideas of unworthiness and delusions of danger concerning her father. She heard hallucinatory voices telling her he was being burnt, but she was otherwise rational.

Physically she was fat, pale with a slight icteric tinge and with an extreme degree of erythema ab igne on her legs. The blood pressure was 98/70, pulse rate 72, the pupils dilated and sluggish in their reactions, the tonsils enlarged and septic, but nothing else of note was discovered. She complained of weakness, dyspepsia and

feelings of numbness in the skin. The urine was clear and sterile ; a urea concentration test gave 3·7 per cent. and 4 per cent. of urea, and the blood urea was 31 mg. per cent.

Tests for syphilis were negative in the blood and fluid. Ephedrine gr. $\frac{1}{2}$, three times a day, was prescribed.

On April 14 a gruel test meal revealed complete achlorhydria. Cultures of the fasting juice gave a growth of streptococcus viridans.

On April 15 the blood count was as follows : red cells 2·8 million ; hæmoglobin, 75 per cent. ; colour index 1·34 ; white cells 11,200. Apart from a mild degree of poikilocytosis, no abnormal cells were observed in a stained film.

Pernicious anæmia was diagnosed, but it was decided to withhold liver for a time and watch for changes in the blood picture.

On April 18 a small inflammatory area appeared above the left knee anteriorly. The blood pressure had risen to 110/80 and the ephedrine was stopped.

On April 20 an incision was made in the inflamed area after spraying with ethyl chloride, and pus was obtained.

On April 22 an area of cellulitis was spreading upwards from the original focus. A further incision was made under gas anæsthesia and a swab taken, from which a pure growth of a hæmolytic streptococcus was obtained on culture. The blood count at this stage was : red cells 2·6 million ; hæmoglobin 70 per cent. ; colour index 1·34 ; white cells 10,400. The film showed poikilocytosis as before and two normoblasts were seen. Two c.c. of Armour's liver extract for intramuscular injection were given and repeated daily afterwards. Hydrogen peroxide syringing and eusol soaks were applied to the wounds.

On April 23 N.A.B. ·45 gm. was given intravenously and 50 c.c. of polyvalent antistreptococcal serum subcutaneously.

The urine was now alkaline, contained albumin and indican, but no urobilin, and an excess of ammonium phosphate in the deposit. Van den Bergh reaction, positive indirect.

On April 24 the cellulitis was still spreading up the thigh, and two further incisions were made under ether anæsthesia ; the original incisions were enlarged and all joined subcutaneously. All pockets were opened and packed with eusol soaks. A further 75 c.c. of antistreptococcal serum was given, the liver injections being continued daily.

On April 26 further incisions were made under ether and joined up as before, N.A.B. ·45 gm. being given intravenously. It was felt that any further operative interference would be useless, and the prospect of recovery appeared most unfavourable. Improvement in the local condition was, however, maintained from then onwards, and by May 2 the infection was obviously subsiding, with a copious flow of pus from all wounds. The blood count showed : red cells 3·7 million ; hæmoglobin 65 per cent. ; colour index ·88 ; white cells 16,600. Two c.c. of liver extract were now given every other day. The urine was alkaline, contained much indican, and urobilin was present. The deposit contained an excess of ammonium phosphate. Improvement continued smoothly and a coincident improvement in the mental condition was observed.

On May 15 ordinary liver extract was given by the mouth in place of the injections, two tablespoonfuls twice a day. The red cells had risen to 3·9 million and the hæmoglobin remained stationary at 65 per cent. The white count was 12,000. The patient remained apathetic and easily tired, but was quite rational and expressed no delusions.

On June 20 the counts were 4·3 million ; hæmoglobin 70 per cent. ; white cells 10,000. Four carious teeth were extracted and two of four cultures of the roots gave a growth of streptococcus viridans, the other two being sterile. The patient was now getting up and the wounds were practically healed.

On August 1 the tonsils were dissected out under ether anæsthesia by Mr. D. MacAlister.

On August 15 the blood count was : red cells 6·1 million ; hæmoglobin 80 per

cent.; colour index ·66; white cells 4,000. The urine was clear and a sugar curve normal.

Because of the relatively mild anæmia and the absence of changes in the blood film and because of the complicating presence of streptococci, liver was now withheld and the patient put on massage, exercises, occupational therapy and tonics, such as iron and strychnine, improvement continuing for some time.

Toward the end of the year complaints of lassitude and depression became frequent, and by January of 1933 it became apparent that the same psychosis with which the patient was first admitted was again developing, the delusions of unworthiness and the fears for the safety of the father being prominent as before.

On January 5, 1933, the blood count was: red cells 3·1 million; hæmoglobin 60 per cent.; colour index ·97; white cells 7,000. Poikilocytosis was present in the film and occasional megaloblasts were found. It was not felt justifiable to withhold liver any longer and two tablespoonfuls of the extract were then given daily.

On February 8 the red cells numbered 4·5 million; hæmoglobin 60 per cent.; colour index ·67. There had been a steady improvement in the mental condition, although the hæmoglobin had remained stationary.

On February 17 a fractional gastric analysis was made following the injection of 1 c.c. of 1/1000 histamine acid phosphate, with adrenalin m. 3 of a 1/1000 solution.

There was no free acid in the fasting juice, but the curve was a normal one for an ordinary test meal, being low for a histamine effect. Streptococcus viridans was grown from the fasting juice.

On February 28 a further gastric analysis following a meal of 50 c.c. of 7 per cent. alcohol was made, complete achlorhydria being found. It was then assumed that had histamine been given at the time of admission, acid would have been found.

On March 10 the red cells numbered 4·3 million; hæmoglobin 70 per cent.; colour index ·81; the film being clear. This was not considered satisfactory, but the patient was feeling so well that her discharge could not be delayed and she was discharged on March 11, 1933, with instructions for her to report if not satisfied with her condition.

On October 13, 1933, she was readmitted as a voluntary patient for a few days, at my request.

She had found work in a factory, and felt well except that she tired rather easily and was greatly worried by persistent tingling in the extremities, information that was volunteered without questioning. An alcohol test meal gave a normal curve, and a histamine curve proved much higher and normal for its type. In both cases there was free acid in the fasting juice. The blood count showed: 4·3 million red cells; hæmoglobin 75 per cent.; colour index ·87; white cells 11,600. The fasting juice was cultured and numerous colonies of a hæmolytic streptococcus were found in the juice for the first time. A vaccine was made from these and sent to her doctor, who has been treating her with it. The patient was warned to increase her liver diet. In February of this year she wrote to say she was improving.

COMMENT

The return and increase of free acid in the gastric juice are noteworthy in this case. The close association of achlorhydria on the one hand and of pernicious anæmia and subacute combined degeneration on the other was first shown by Hurst and Bell,[25] who also suggested the importance of hæmolytic streptococci in the intestinal tract. Exceptions have occurred; Wilkinson[26] gives a fairly long list of cases to date where free acid was

present in the gastric juice, but it is sufficiently rare to call the diagnosis into question. Hurst,[27] Connery and Joliffe [28] and Davidson [29] have reported instances of the return of acid following treatment.

Vaughan states that the therapeutic action of liver is seriously inhibited by the presence of sepsis, and this may explain the rather slow response in this case.

The mental state was a mild melancholia with some confusion. The return of symptoms in the absence of liver treatment was striking, but improvement took place before any rise in the hæmoglobin content could be demonstrated.

Case II.—J. H. P., male, age 57.

The patient was a labourer and had been a cheery, bluff, garrulous man. There was a fairly strong history (obtained from his wife) of prolonged alcoholism, although the patient only confessed to an occasional glass of beer. His health had been generally good, but two years before admission he had had a total extraction of his teeth because of their foul condition.

One year before admission he began to be troubled with pins and needles in the feet and legs, and five months later complained of weakness of the legs. During the following two months he was treated for myalgia with no benefit. He then attended a hospital and blood was taken from a vein for examination, but no change was made in the treatment. His wife watched the development of failing memory, drawling speech, general lassitude and marked irritability. His appetite became poor and he lost weight, finally becoming bedridden with extreme weakness and drowsiness and complaining of intense headaches. Fourteen days before admission he was removed to a Poor Law Hospital and his case diagnosed as a Korsakoff's psychosis from alcoholism, being admitted to the Mental Hospital with this label on June 1, 1931. Mentally he represented a typical Korsakoff case with marked loss of memory for recent events, coupled with complete disorientation in time and space, confabulating freely and confidently when questioned, due allowance being made for his weakness and drowsiness.

Physically he was emaciated, with bedsores on sacrum and buttocks. The skin and mucous membranes showed a marked pallor, but the cheeks were high-coloured, and there was a slight general icterus. The tongue was red, glazed and dry. There was a cardiac hæmic murmur and the pulse was rapid and weak. Coarse moist râles were present over both lungs. Muscle power was fairly good, but there was incoordination in all limbs, and the legs were spastic. Coarse muscle tremors occurred irregularly. Joint sense was diminished in the feet. The abdominal reflexes and the knee- and ankle-jerks were absent, the plantar reflexes indefinite. There was no skin anæsthesia and no deep tenderness. The pupils were normal.

Tube-feeding was instituted, and because of a mild delirium developing at night mild sedatives were ordered. On June 4 the Kahn test was negative in the blood and fluid. The blood urea was 21 mg. per cent. The urine was acid and contained albumin, acetone and indican. A confident diagnosis of alcoholic polyneuritis led to a regrettable delay, and it was not until June 7, while the case-details were being written out from a notebook, that the truth became apparent. On that day a blood count showed : 1·6 million red cells ; 45 per cent. hæmoglobin ; colour index 1·41 ; white cells 6,000. A film showed marked poikilocytosis and polychromasia with frequent normoblasts and megaloblasts. The Van den Bergh reaction gave a delayed, direct positive and the urine contained urobilin. On the same afternoon 1 c.c. of Armour's liver extract for intramuscular injection was given intravenously by mistake, but without any ill

effect, and another 1 c.c. was given subcutaneously. Ordinary liver extract was commenced in doses of two tablespoonfuls three times a day. On June 14 there were 1·9 million red cells ; 52 per cent. hæmoglobin ; colour index 1·37 ; white cells 5,600 ; on June 22, 4·1 million red cells ; 60 per cent. hæmoglobin ; colour index ·97 ; white cells 8,800. The progress in general health was remarkably rapid, and on July 6 the red cells numbered 4·2 million ; hæmoglobin 80 per cent. ; colour index ·95. The bedsores were healed, weight was increasing, and the patient was sitting up in bed very jovial and very garrulous.

On July 17 the count was : red cells 5·3 million ; hæmoglobin 80 per cent. ; colour index ·75 ; white cells 4,400. The film appeared normal. The mental improvement was definite, but lagged behind the improvement in general health, while the paralysis of the legs remained severe.

On August 8 the red cells numbered 6·3 million ; hæmoglobin 105 per cent. ; colour index ·83 ; white cells 9,000.

A test meal showed no free acid in the resting juice or in the first three tubes, but no further specimens were obtained owing to active resistance on the part of the patient.

He was now normal mentally and physically, except for the incoordination of the limbs. The knee- and ankle-jerks were still absent, the right plantar reflex extensor and the left flexor.

Massage and exercises effected a great improvement in his condition, and on May 20, 1932, he was discharged from hospital, walking with difficulty.

On December 13, 1933, in response to an enquiry, he wrote that he felt wonderfully well, but was rather weak from the knees down, although he could get about fairly well.

COMMENT

This was a straightforward case, but the Korsakoff syndrome was unusual. The diverse origins of such syndromes are, of course, well known ; cases have been described due to intoxication from arsenic, lead, mercury, tuberculosis, diabetes, influenza, typhoid fever and erysipelas, and also occurring in encephalitis lethargica, malaria, ruptured cerebral aneurysm, and other conditions, as well as alcoholism. In this case, with no pernicious anæmia and a little more alcohol, he might well have developed a pure alcoholic Korsakoff's syndrome.

These two cases support the view that the mental changes developing in pernicious anæmia depend on the state of the psyche when the disease develops. If the disease becomes severe enough, a toxic confusional state is produced. The treatment is mainly that of the anæmia.

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TRAUMATIC ENCEPHALOPATHY (' PUNCH DRUNK ') OF PROFESSIONAL PUGILISTS*

By

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The result, immediate or remote, of repeated injuries to the brain of a professional boxer forms a study all in itself, and contrasts with the more usual sequelæ seen when patients have received only one injury in the course of industrial or other pursuits. The problem, moreover, forms one phase of the extremely complicated and highly controversial subject of head injury and its consequence. For purposes of description, the injuries received by pugilists in activities of their profession may be divided into those received during an actual bout, serious enough to cause death immediately or a few hours later, and those which more by their repetition than by their severity lead to slower development of disability during the fighter's career. It is with this latter group that this paper is concerned.

Martland, in 1928, drew attention to the various mental and physical states encountered in examination of former pugilists, and under the title of ' punch drunk ' outlined some interesting clinical syndromes. He assumed that the condition afflicted, in mild or severe form, at least 50 per cent. of pugilists of a certain type who had kept at their profession over a certain period. It is not so common among successful pugilists who reach their eminence by rapidly disposing of their less expert adversaries, with but little injury to themselves. Quick, agile, clever boxers who guard themselves well and take little punishment seem to escape. Chiefly affected are the less expert but courageous men who take considerable injury in the hope of wearing out their opponents until they can get in a final knock-out blow, and those used for training, who are accustomed to be knocked down several times a day. Aggressive, hardy fighters who like to give the crowd an exhibition of blows, and who lead the fight to the end, are likely to suffer, and the degree of facial disfigurement is the index of the susceptibility to ' punch drunk.' According to Martland, the early symptoms of the disease are represented by occasional clumsiness of one foot, seen in walking to the corner of the ring, slight ataxia and periods of confusion; at this stage ability to fight may not be seriously impaired. Many cases are mild and do

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not progress, but in the more severe types the legs drag in walking, and tremors, dysarthria, deafness, physical slowing-up and even mental deterioration which requires commitment to an institution may supervene. It is thus possible that a pugilist may be only mildly affected, and may continue to fight to the end of his career, or he may be so disabled that he ultimately has to quit boxing and yet gets no worse in after life. Lastly, a progressive neurological syndrome may appear, putting an end to all fighting, and leading finally to mental or physical helplessness. It is well understood, moreover, that pugilists are not immune to the ravages of syphilis, alcohol, or even epidemic encephalitis, and certainly the incidence of these diseases is no lower among pugilists than in the general population. The point that Martland urged, however, was that the high frequency with which professional pugilists develop crippling disease of the central nervous system of one sort or another suggests a result of the repeated injuries to the brain that they received while carrying on the activities of their profession. Figures which disclose the frequency of disability among former pugilists unfortunately are not available, but the investigation that Martland made suggests that it is relatively high. In the hope of further elucidating the problem, some new material is presented as an argument for the existence of such a condition as ' punch drunk ' or traumatic encephalopathy and illustrating some of its very variable clinical features.

REPORT OF CASES

Case I.—A man, age 24, came to The Mayo Clinic on February 9, 1934, because of weakness of the legs and tremor of the hands. There was no family history of similar disease. He had had influenza in 1922 ; it was not severe, and he was in bed only a few days.

At the age of 15 he had commenced to box, at first as an amateur. He had become a professional pugilist at the age of 16, in 1926. In that year, in the course of a boxing match, he had received a blow over the left temple, which had knocked him down, and blood had run from his left ear. From 1926 to 1931, he had fought as a lightweight and had averaged about two fights a month. He had made no great headway in his profession, for he had lost as often as he had won and he had not improved his technique greatly. He was not a very good boxer, although he was willing to take considerable punishment in the hope of getting a final victory by knocking out his opponent or wearing him down. He had been knocked unconscious many times, but only for short intervals. One time he had finished eight rounds after being knocked down and had no subsequent memory of it. In 1929, he had been knocked down five times, but he had not been knocked unconscious ; the referee stopped the fight. The patient usually made little effort to guard himself, and as a consequence he had a flattened nose and two ' cauliflower ' ears. In 1931, he was told by his manager that the chances of his rising in his profession were slight, and, opportunities of getting good matches becoming less and less, he decided, in 1931, to retire from the ring and became a filling-station attendant. He felt well during that time. In April, 1932, the chance of making money from a bout presented itself and he re-entered the ring. He was knocked down twice in the third round, once by a blow over the right side of his jaw and the other time by a blow over the left eye and temple. He took the count of nine and then finished the fight of six rounds. Imme-

diately after the fight, he felt as usual, but a few minutes later he took a drink of water, which he promptly vomited. He continued to vomit and retch, even on an empty stomach, and an hour after the fight, when attempting to go home, he reeled and staggered as if drunk. He managed to make his way home, and went to bed, but slept poorly because of nausea. Finally he slept and awakened at 10 a.m. When he attempted to arise he found himself very unsteady and was unable to balance himself. He was able to walk after a fashion, and actually had more difficulty in equilibrium than during the previous night. After consulting a physician, he returned to bed, where he stayed for three days, feeling nauseated and complaining of diplopia. He improved somewhat after this rest, and again he arose, but, while the diplopia had disappeared, he was still unsteady, although very much less so than previously. In two weeks he returned to his duty as a filling-station attendant, still slightly ataxic.

Two months later, in June, 1932, chance of another fight had come to him, and, in spite of his poor balance, he thought to train for it and overcome this difficulty. While in training, his legs seemed to get worse and he found that he tired very readily. He seemed to be fast enough on his feet in the ring at the beginning, but was unable to endure any considerable length of time, because of a sense of fatigue of his lower extremities and a tendency of them to drag. He had given up the idea of fighting.

From that time up to his admission at the clinic (1934) his condition had changed little. When I first saw him he still had trouble in walking, in that his feet seemed to drag. The right foot was worse than the left and he wore away the toes of his shoes. The sense of balance was not normal, but slightly better than it had been; yet he frequently staggered, more at times than at others. By conscious attention to walking he would pick up his feet better than he usually did, but he soon relapsed into a dragging gait. His mother complained that he was more nervous since his last fight, a little more forgetful of names and details, and that his hands shook. Under excitement, he tended to have a general tremor.

The patient was well developed and muscular, weighing 120 pounds (54·4 kg.) and showing obvious signs of his previous profession in the form of thickened auricles and flattened nose. His systolic blood pressure was 130 mm. of mercury, and his diastolic 76. He walked slowly and unsteadily. His lower limbs were stiff and slow, the right being the worse of the two. At the same time, he staggered on turning suddenly and was somewhat ataxic. He held the right arm flexed when walking, and stiffly at his side, and did not swing it like the other. He hopped clumsily on the right foot, but did better with the left. The toes of both shoes were well worn down. There was a coarse, pill-rolling tremor of both hands, more marked on the right. Slight tremor of the head was present, but speech was unaltered. Speed was diminished on the right side, in both the upper and lower extremity, especially for rapid movements like drumming with fingers on a table. All tendon reflexes were greatly exaggerated, but there was no Babinski's sign on plantar stimulation. Romberg's sign was positive, and slight, horizontal nystagmus was present. Facial expression was normal and labile. Urinalysis and examination of the blood disclosed nothing abnormal, and the flocculation test for syphilis performed on the blood was negative. X-ray studies of the skull gave no evidence of fracture or other abnormality.

COMMENT

There is but little doubt that the severe beating received by this pugilist in his last fight was responsible for the chain of circumstances which followed. Although he finished the fight, the symptoms which appeared almost immediately thereafter suggested at least moderately severe injury to the brain, from which he made very far from complete recovery. It might also be

suspected that his previous experiences had altered him so that he was an easy victim in his last fight, but of this there is no evidence, and he attributed all his difficulties to his last and futile appearance in the ring. The unbroken chain of cause and effect is very evident in this case, and it is to be noted that in nearly two years the condition had not become worse nor was there much improvement beyond a certain point. Clinically, the picture was a mixed one, suggesting multiple lesions involving the cerebellar, corticospinal, and basal ganglia systems of motor control. No specific nervous syndrome appeared, such as Parkinson's disease, but rather a medley of scattered and incomplete lesions of the brain.

Case II.—A man, age 30 years, came to The Mayo Clinic on January 9, 1928, because of difficulty in walking and in speech. There was no history of any similar condition in his immediate family. He was married and had one child who was living and well. He had had practically no illnesses before the condition concerning which he made his complaint, although he admitted having had minor infections of the respiratory tract, which at no time had necessitated confinement to bed. He denied having had syphilis. He had commenced boxing at 16, in 1914, and shortly thereafter he had become a professional pugilist, fighting more or less continuously up to 1921. He had ranked as a second-rate boxer, and although he had demonstrated plenty of courage and had taken considerable punishment, he never had reached professional eminence. He had the usual broken nose and thickened ears of his trade.

On March 4, 1921, he was knocked out in a fight. He was unconscious during the count of ten, and unable to get up a few seconds later. He mentioned that he had received the blow on the left side of the lower jaw and that it was sufficient to put him out quickly. He walked out of the ring, however, rode home in a street-car, and, angered by his defeat, proceeded to get drunk, but finally went to bed. The next day he seemed normal, and then had started training for the next fight which was to take place 16 days later. During this period of training he noticed that, when he was skipping rope, his right leg tended to catch on the rope, but he took little notice of it at the time. In the subsequent three fights which he finished, he had been winner in the first, and had fought the other two to a draw. The fourth fight was in June, 1921, and it proved to be his last. He was knocked down by the first blow of his opponent, which was a moderately hard one, and when he attempted to get up he was dizzy, had a severe headache, and promptly gave up the fight. While walking home, he found that the difficulty with his right leg had become decidedly noticeable; both lower limbs felt numb and they dragged as he walked. He decided, after this, that he was no longer fit to fight in the ring, and became a labourer in a steel mill. During the first month that elapsed after his last fight, and while he was working in the mill, the stiffness and slowness of movement of his lower extremities increased. This was more marked on the right side, for, as time went on, he wore out two soles of the right shoe to one of the left. Walking became increasingly difficult; he noticed that his voice had become nasal, and that articulate speech was becoming more and more indistinct. He continued at the mill about 18 months, when he was discharged because his infirmity had become obvious.

In the latter part of 1923, movements of the right arm became stiff, clumsy, and awkward. Spasmodic contractions of the muscles of the right arm, right leg and back appeared and gradually increased so that in walking he felt a tendency to be pulled backward. He had occasional parietal headaches lasting from one to four hours, and his powers of mental concentration, attention and memory were considerably reduced.

Through the subsequent four years, his difficulties slowly and gradually increased. He experienced more and more difficulty in walking and in speech, as well as increasing spasms of the muscles of the extremities and trunk. At the time of his examination, however, he still was able to walk alone, and he could feed and dress himself.

The patient was well nourished, weighed 130 pounds (59 kg.) and there were no abnormal physical findings apart from those suggesting disease of the nervous system. Urinalysis, blood count, examination of eye grounds, and the Wassermann test revealed nothing unusual, and the same result was obtained from X-ray studies of the skull and cervical portion of the spinal column. Neurological examination gave a complex picture.

The man was of unusual muscular development, probably because of his profession and training, and this rendered more conspicuous the various contractions and spasms continuously at play in his muscles. In walking, his gait was unsteady and spastic; the spasticity was more marked on the right than on the left side. More conspicuous, however, were the continuous, irregular spasms of the muscles of the right arm and back. These were sufficiently violent to pull the man backward and to the right, with the right arm jerking and his hand slapping his thigh. These contractions were rapid, ever changing and quickly repeated. When the right arm was extended forward, fully supinated, continuous jerking occurred, tending to flex and pronate the arm. When, on the other hand, the arm was drawn behind the trunk in full pronation, these movements ceased. While the patient was seated the muscles of the back were continuously jerking, pulling him backward and to the right. The muscles of the neck and face were quiet. There was no paralysis, but all of the man's movements were slow and clumsy, except when he was running and jumping, which acts he performed, on the whole, better than slow walking. When he was asked to perform rapid movements of the fingers, these movements were slow on the right side, but in the left leg and foot the movements were equally slow and spastic. The tendon reflexes on the left side were exaggerated, and plantar stimulation on the left side produced an extensor reflex. Stroking the lips with a hard object produced a sucking reflex (Oppenheim's sign). Tests of coordination, applied to the upper and lower extremities, did not disclose marked dysmetria or dyssynergia, but all tests were interfered with by the irregular, spasmodic contractions. There was no nystagmus. Speech was very indistinct, slow, laboured, grating and nasal in tone, and the breath escaped through the nose while the man was talking, apparently because of some weakness of his soft palate. During animated conversation, he had the tendency to break into a silly guffaw. This, with the mouth wide open and with the tone of voice, seemed to suggest the spasmodic laugh seen in pseudobulbar palsy or progressive lenticular degeneration. Mentally the man seemed childish, and below par even when his social standing and previous education were discounted. He was written to and a reply was received dated March 22, 1934. In this letter he stated he was still able to get around, had not become any worse, and, if anything, there was a slight improvement during the six years that had elapsed since his examination at the clinic.

COMMENT

Again, as in Case I, this patient was a plucky and aggressive fighter, but of no great eminence in his profession; he was a lightweight, who started to fight when quite young, took plenty of injuries, and ended disastrously. However, the clear-cut chain of events existing between cause and effect is not so obvious in this case. All that is known is that after seven years of strenuous fighting and during the course of his career, between one bout

and the next, symptoms appeared insidiously, increased in severity, and put an end to his fighting. Even after he had left the ring and had tried other pursuits, his difficulties increased steadily up to the time he appeared at the clinic, seven years after his last fight. Argument could be advanced in this case that his trouble was due to a chronic phase of epidemic encephalitis and that the initial episode, in the form of a mild respiratory infection, had passed unnoticed. In Parkinson's syndrome of epidemic encephalitis the initial episode may be absent or so mild that it is even forgotten, and yet the disease appears and progresses steadily to complete disability. It is, however, begging the question to assume that this patient had epidemic encephalitis, for this is incapable of proof, and it is just as plausible and reasonable to assume that repeated injuries to his brain led to a progressive, bizarre syndrome of disease of the nervous system. Moreover, the clinical picture was exceedingly complicated and did not resemble at least the more usual sequelæ of epidemic encephalitis. There was, first, evident dystonia, producing grotesque muscular contractions, but the corticospinal motor system was affected also, as shown by the spasticity and Babinski phenomenon. There was also the dysarthria and the spasmodic laugh to account for, and altogether the picture was that of scattered and diffuse lesions of the brain, resembling no specific clinical syndrome. In the final analysis, and unsupported by necropsy, it can only be a matter of opinion that this patient's trouble was due to his pugilism, but in view of other cases reported a strong feeling remained that it was actually due to this.

Case III.—A man, age 28, came to The Mayo Clinic first on March 23, 1923, because of stiffness and dragging of his legs in walking, unsteadiness of gait, and indistinct speech. There was no family history of similar difficulty, and the patient had had no previous illnesses requiring confinement to bed. He admitted having had gonorrhœa several times, and that he had had a sore on his penis at the age of 17, the nature of which was uncertain.

He had started as a professional pugilist at the age of 18, and had fought steadily, up to the time of his admission, i.e, for ten years. He had had as many as three fights in one week, and five fights in one month ; in one year he had fought 22 times. He had served in the army during the war and had boxed several times. While serving as a mess waiter, just before his discharge in 1919, he noticed that his left hand and foot were clumsy ; he spilled glasses of water because the left foot hit the ground awkwardly and the hand shook. He thought nothing of it at the time. On discharge from the army he immediately had gone back to professional boxing, and had continued to hold a championship until he lost it because of an adverse decision. During the latter part of 1919, while walking with his friends, they jeered him because his left leg hit the ground with a slapping noise, and for the first time he realized there was something wrong. Nevertheless, this had not interfered with his ability as a boxer at that time. In 1920 episodes of staggering while walking in the street appeared, and his speech became thick, so that he was accused unjustly a number of times of being drunk. Just before one fight a ring attendant, after talking to the patient in his dressing room, insisted on calling the manager to stop the fight, because he thought the fighter was intoxicated. The patient had won that fight after a terrific battle. Gradually, during 1921 and 1922, the increasing stiffness of the left arm and leg and

the unsteady gait became more obvious. He would be slow, awkward and clumsy in the first few rounds, would spar for time, then, becoming heated and loosened up under the influence of exercise and excitement, would finish as well as ever. The left arm would go into clonus, puzzling his opponent by its unexpected and grotesque trepidation, and then the right arm, which never had become affected, would do its deadly work. Nevertheless, remorselessly his disease advanced, speed and precision were slower in appearing with each bout, and a few days before the patient's first visit to the clinic his career ended in an inglorious fashion. He had been pitted against a boxer whom he easily had beaten before, and had expected to beat again. In the first few seconds of the first round, while still stiff and awkward, he was given a slight push, stumbled and fell and was unable even to get back on his feet again. While the crowd howled in derision his seconds threw in the towel and his last fight was over.

As a boxer he had been of the aggressive type, fast enough in action, but he had disdained to guard himself much, and had carried the battle into his opponent's quarters continuously. He stated that he hardly ever had felt the blows he received, never had been knocked out, but had received many terrible beatings, winning in the end by his superior stamina and ability to stand up under heavy punishment. He never had to go to bed after a fight, in spite of many cuts and bruises received around his face and head. He belonged to a certain school of prize fighters and was the only one affected among his crowd. As a possible explanation was the fact that they were all fast, clever boxers, hard to reach with a blow, and of them all he was by far the most disfigured and had a particular reputation for being a hard fighter. He had had innumerable Wassermann tests of his blood, all with negative results, and at least several examinations of spinal fluid, not one of which had disclosed evidence of syphilis.

When he was examined in 1923 his disability was obvious. His speech was thick, muffled and hard to understand ; there was a rasping, laboured quality in the voice. His gait was spastic. The spasticity was marked on the left side, and he dragged his legs, wearing out the toe of his left shoe. There was no marked weakness. The grip of the left hand was weaker than that of the right, but the outstanding feature was the slowness and clumsiness of the fingers, hand and arm. In certain positions the left arm went into clonus. Patellar clonus was also present, and there were a few strokes of ankle clonus on the left. Tendon reflexes were everywhere enormously exaggerated, more so on the left, and on that side a Babinski phenomenon could be elicited. The jaw reflex was exaggerated, and sucking reflexes were present on stroking the lips. The man was unable to hop on the left leg, and on performing active movements, such as shadow-boxing, he was so stiff and clumsy that he nearly fell, and his left arm was slow and awkward. The right arm and hand seemed but little affected. There were no sensory changes, tremors or nystagmus ; facial expression was mobile and pupillary reactions were normal. He seemed below par mentally ; his general intelligence and his memory were somewhat reduced. Facial disfigurement was extreme ; both ears were thickened and shapeless ; his nose was flattened ; his eyebrows were thickened and full of scars, and his lips were irregular and distorted ; many front teeth were missing. General physical examination disclosed nothing more. The Kolmer modification of the Wassermann test, applied to the blood, gave negative results. On examination of the spinal fluid, the Wassermann reaction was negative ; the Nonne test was negative ; 1 small lymphocyte was present per cubic millimetre, and the colloidal benzoin test gave no curve.

A diagnosis was made of lateral sclerosis of the spinal cord, and some doubt was expressed as to the origin of the condition. Syphilis was suspected because of the history, and a course of antisyphilitic treatment was advised on empirical grounds. A very poor prognosis was given, since it was expected that progression of the disease could be expected. The patient was lost track of thereafter, until, for the purpose of the present investigation, he was written to, and in response he reappeared on

March 7, 1934, almost exactly eleven years after his first examination. To our surprise we found that time had dealt gently with him. He seemed in no way worse, and beyond acquiring a certain amount of obesity he presented an identically similar picture to that encountered on his first examination, and was, if anything, somewhat improved, discounting the increased weight and lack of training. His disturbance of speech and gait were as conspicuous as before, but he had not deteriorated any more, physically or mentally. He had taken no antisyphilitic treatment in the meantime, and had added to his collection a few more negative Wassermann tests on his blood and spinal fluid. He had been engaged in various occupations, mainly sedentary, had been moderately successful, and seemed at peace with the world.

COMMENT

Here the picture is somewhat different from that encountered in the other two cases. The patient, a high-grade pugilist, developed symptoms during a period of four years, coincident with his heaviest fighting. The symptoms slowly progressed up to his final, ignominious failure in the ring, and then, for eleven years thereafter, his condition remained much the same as it was when he ceased fighting. The picture was also different from that presented in Cases I and II; it was mainly that of injury to the corticospinal motor tracts on both sides; hence the original impression of lateral sclerosis. The man's frank admission that he had contracted venereal disease further led to the presumption that he had syphilis, but this was never proved, either serologically or by any clinical finding that was specific for syphilis of the central nervous system. It is reasonable to exclude this disease in its entirety, and more logical to blame the innumerable injuries to the brain received at the height of the patient's career.

Jokl and Guttman have recently reviewed the subject of symptoms referable to the central nervous system presented by pugilists. They divide the symptoms into three classes: those appearing in the course of the actual bout; those coming on some hours or days thereafter, and those appearing in the later life of the pugilist. The latter they divide into mental and physical. Mental deterioration, they think, can afflict patients who are predisposed to it even before they enter the ring, but they also think a definite dementia affects former pugilists as a result of cerebral trauma received during their careers. On the physical side, Jokl and Guttmann describe changes in tendon reflexes, dysarthria, disturbances of coordination and anomalies of speech.

SUMMARY AND CONCLUSIONS

Three cases of chronic disease of the nervous system, affecting professional pugilists, have been described. In the first, the maximal functional disability appeared immediately after a fight, improved somewhat during the next few weeks, but thereafter remained at a standstill. In the second case the progressively crippling syndrome appeared insidiously during the

last few fights of the patient's career. His difficulties had progressed up to the time of his examination four years later, but apparently had not become worse, and were, if anything, improved in the subsequent six years. The third patient also gave evidence of the insidious development of an affliction of the central nervous system appearing five years before he ceased to fight and progressing up to the time of his leaving the ring. However, after the patient's fighting career was over his condition remained stationary or perhaps improved slightly. The clinical picture in each case was very complex and it differed in the one case from the others. The only agreement, however, was in the suggestion of diffuse or scattered lesions of the brain affecting different systems at one and the same time. It is assumed that these patients' difficulties resulted from repeated injuries to the brain received during their pugilistic careers. If probabilities are to be discussed, the first patient was without reasonable doubt injured during his last fight and his subsequent difficulties resulted from it. In the case of the third patient, his difficulties appeared during his fighting career but stopped progressing as soon as he left the ring. The probability here, that his disease was connected with his occupation, is good. The case of the second patient must remain in doubt, for there was not the clear-cut association between his occupation and his disability. Since postmortem study is lacking, the exact pathological mechanism of these cases is to date unknown. The fortuitous occurrence of epidemic encephalitis or syphilis of the nervous system during the pugilist's career cannot be excluded as a cause of the difficulty. However, the frequency of occurrence of conditions of this kind as reported by others among people who followed the profession of pugilism makes it seem very likely that their profession led to their ultimate disablement. It is to be hoped that in the future more statistical data, backed up by pathological studies, may put these conclusions on a firm basis.

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CALCIUM IN EPILEPSY

By

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INTRODUCTION

The possibility that the epileptic crisis may be associated with some disturbance of calcium metabolism has attracted many workers. My attention to the problem was aroused by an accidental observation in a girl of nine years old, who had cycles of 60 to 100 fits monthly for three or four months, and was then comparatively free for a similar period. Towards the end of one of the fit-cycles she was asthenic and dull, and her ribs had become so soft that they were bent out of shape by the pressure of her arm as she lay in bed. She showed the signs of Chvostek and Trousseau, but had no other symptoms of tetany. Unfortunately, the serum calcium was not examined at this time. As she became stronger after the end of the fit period the softness of the ribs and the deformity disappeared.

Investigations of the serum calcium content in epileptics have been made by several workers, and the findings have usually shown it to be within normal limits or at the lower level of normal values. Lennox and Allen, making single observations on 77 epileptics, found an average of 9·79 mg. per 100 c.cm. of serum, as against a normal average of 10·067 mg. Parhon and Ornstein in 35 cases found values at or below the lower limit of normal, which they considered to range from 10 to 12 mg. per cent., only two of their cases showing higher values. Madsen, with repeated determinations on a group of patients, found an average of 10·4, as against a normal average of 10·8 mg. per cent., but he noted a very much wider range of variability. His figures showed marked individual variability also. He has given details of the relation of his findings to fits in some cases, showing mostly high values before and during runs of fits, and a low value after a run of fits, but he does not state the times of the fits. He found the Ca/Na ratio normal, but excess of Ca in the Ca/K ratio. Hamilton, in his study of the inorganic constituents, found in 19 estimations that the serum calcium ranged from 9·6 to 12·8 mg., and the phosphorus from 2·6 to 6 mg. Osnato and Killian, in a similar study, found in 19 estimations serum calcium values from 9·5 to 12·8 mg., with an average of 10·9 mg., and phosphorus values in 11 cases from 2·5 to 4·5 mg. Other workers have considered the question of the ionic state of the calcium, calculating the free ions from the *p*H of the blood and the alkaline reserve. Bigwood, in several studies, has found a rise of alkalinity and a consequent fall in calcium ions preceding a fit. Di Renzo, however,

by similar methods found a rise of alkaline reserve till an hour before a fit, then a sudden fall, suggesting an increase of calcium ions preceding the attack.

Many of these findings are not harmonious, and additional information that would be relevant is meagre or absent. While details are given in some cases, the time of the fit is not recorded, nor is the relationship of the fit to other attacks. In several cases only interparoxysmal estimations are recorded. Also, much of the work has been done on chronic institutional cases.

Several investigators have reported the results of calcium treatment by mouth or intravenously. Petzetakis was convinced of the great improvement in two cases treated with intravenous calcium chloride, which he found to inhibit the fit. Klein and Forcione found no improvement, but rather a tendency to increase of fits in cases treated by intravenous calcium, though in their cases luminal had been discontinued for the period of the experiment. Hopkins Detrick considered that calcium treatment reinforced by methods for raising the calcium content of the blood was of value in all types of cases.

PERSONAL STUDIES

It seemed to be worth while to make a fairly large number of repeated observations of serum calcium on a group of young epileptics, who were living a normal school and out-door life on a colony. Samples of blood were taken at various times of the day and at varying intervals over a prolonged period, in the hope of obtaining a sufficient number of observations to be able to correlate them with the time of the fits, which are all recorded in detail as a routine. The cases chosen were nearly all those of young males from 10 to 25 years old, not mentally defective, and with various types of fit and fit incidence. There was no change in their routine or diet except for occasional experiment. The chief difficulty was to obtain samples of blood immediately before a seizure or group of seizures; in 540 estimations only one was less than five minutes before the fit. There was also difficulty in obtaining the samples in relation to fits occurring at night; when blood was taken during the night the subjects had no fits.

The estimations were made on 48 individuals, two only being girls, on whom six observations were made. The method used was that of Kramer and Tisdall, with, as a rule, 2 c.cm. of serum. Duplicate estimations were frequently done, with a difference of never more than 0·2 mg. in the result. The estimations were all carried out by the same person and as far as possible under the same conditions, at least eight being done in a batch. Some 433 estimations were made on serum separated from the clot after standing overnight; in the remaining 108 the serum was expressed by immediate centrifuging, so that estimations of serum phosphorus might be made on the same sample. As a control 16 samples were split, and half centrifuged immediately

and the rest left to clot overnight. Of these, in nine cases the value obtained from the serum from overnight was higher than that found by immediate separation, in three cases lower, and in four about the same. The average values obtained from the immediately separated sera were found to be about 0·5 mg. lower than those from sera obtained by standing, and the range of values wider, and the former values have therefore all been ignored in the results now to be recorded.

From a total of 433 estimations of serum calcium an average reading of 10·126 mg. per 100 c.cm. was obtained. This lies within the normal limits of 9·5 to 11 mg., and agrees fairly closely with the findings of other observers. The range of values, however, was found to be wide, as shown in the appended table.

TABLE I. RANGE OF SERUM CALCIUM

Between	6 and 7 mg.	3 cases	0·7 per cent.
	7 8	7	1·62
	8 9	40	9·47
	9 10	123	28·41
	10 11	166	38·33
	11 12	79	18·24
	12 13	13	3·33
	13 14	1	0·23

The majority of readings are within the normal range. The variability in range is found in individuals as well as in the whole group. In 22 subjects the range was small, within the limits of 2 mg. per 100 c.c.; in six of these the values lay wholly below 10 mg., while in four the range was wholly above this figure. In 17 individuals the variation is much greater. I could find no correlation between the range of values and the frequency or type of fit.

In correlating the serum calcium findings with the occurrence of seizures, it was found impossible to make a constant correspondence in individual cases, but by averaging the readings some correlation appeared when considering major fits only.

TABLE II. CORRELATION OF VALUES WITH FITS

Fit-free interval	205 readings	average 10·032 mg.
Within 48 hours before fit	87	10·162
Within 48 hours after fit	102	10·056
Between two fits, within 48 hours of either	39	10·718

In this table we see that the average value before fits is slightly but definitely higher than after the seizures. The highest figure, obtained between fits at close intervals or during a series, is striking and unexpected. Actually, in 23 of the 39 values so obtained, the figure was over 10·5 mg., and in several cases over 12 mg. In two cases, however, when blood was taken during a series of fits which proved fatal—one in a girl and one in a boy—the values were 8·8 and 8 mg. respectively, in marked contrast to the other findings. Readings after a run of fits proved to be low in many cases; values from 6·2 to 8·8 mg. were obtained from seven cases under these circumstances.

An attempt was made to correlate the serum calcium findings with the usual time of the fit in individual cases. The subjects were divided into groups of (1) those with fits by day or by night only, (2) those with fits either by day or night, and (3) those who tend also to have fits during the waking period (taken as from 6 to 7 a.m.). The results are given in Table III.

TABLE III. RELATION OF CALCIUM WITH USUAL TIME OF FIT

Group by time of fit	Fit-free interval	Average 48—24 hours before fit	Average 24 hours—time of fit	Average up to 24 hours after fit	Average 24—48 hours after fit	Between two fits
Day only (15 cases)	10·06	9·74	10·12	9·74	10·55	11·3
Night only (14 cases)	10·07	10·08	10·33	9·83	10·3	10·5
Day and on rising (6 cases)	9·74	10·56	9·95	10·21	10·4	11·3
Night and on rising (5 cases)	10·14	10·32	9·76	10·31	10·35	10·24
Mixed day and night (8 cases)	10·09	10·37	10·15	10·17	10·48	10·3

In this table the very close correspondence of the values in the fit-free interval is noticeable. The groups who have fits at the rising hour show a reversed behaviour of the calcium before and after fits as compared with the groups who do not have fits at these times, the postparoxysmal values being higher than those before fits instead of lower as in the other groups. No regard of the actual time of the fit was taken in making this correlation. Where, however, the figures for each hourly interval before and after fits are examined, a definite difference in the behaviour of the serum calcium is disclosed according as the fit occurs during the day or the night. Figures for the rising hour were insufficient to warrant any conclusion, while in the hourly series some inevitable blanks occur. With fits during the day the average values from 48 to 20 hours before the attacks are high; then, till about four hours before, they are definitely lower; then there is another rise till

during the last hour before the fit there is a drop of 1 mg. in the average figure; this lower value is maintained during the hour following the fit, followed by a period of high values for about 14 hours, then relatively low values till a 'normal' level is reached about 36 hours after. When the fits occur during the night, however, the periods of low and high values appear to be almost completely reversed, but I have no figures nearer than three hours from the paroxysm. In Chart I this curve is shown with averages calculated for six-hourly periods.

The actual values obtained within one hour of a fit, occurring during the day, are given below.

TABLE IV. ACTUAL CALCIUM VALUES WITHIN ONE HOUR OF A FIT

45 minutes before a major fit	12	mg. (in a series)
4 minutes before	6·8	
Fit occurring while blood taken	10	(in a long series)
	9·4	,, ,,
10 minutes after fit	10·8	
	11·9	
	8·8	(in a fatal series)
30 minutes after	10·5	
	8·5	(a case with low Ca)
50 minutes after	10·2	
	11·4	(in a group)
	10	
	9·6	

In one case of special interest the readings obtained in the free intervals were unusually constant, the value on six occasions being 9·4 mg. In this case, 27 hours after a group of fits arising during the day, a value of 7·4 mg. was obtained. A reading of 10·4 mg. was obtained three hours after a fit in a group starting at night; and on three occasions, 10 to 40 hours after groups of fits during the night, the relatively high values of 10·4, 10·7 and 10·3 were found. This case strongly suggests that there is some metabolic difference between fits occurring in the daytime and those that occur at night.

A few estimations were taken between 1 and 2 a.m., when the patients were asleep. In four cases readings were low (8·4 to 8·8 mg.), and in two of these, fits occurred during the following night. In four other cases readings were 9·4, 9·8, 10·1 and 11 mg. In the last case a fit occurred at 6·5 a.m., 28 hours after the blood had been taken.

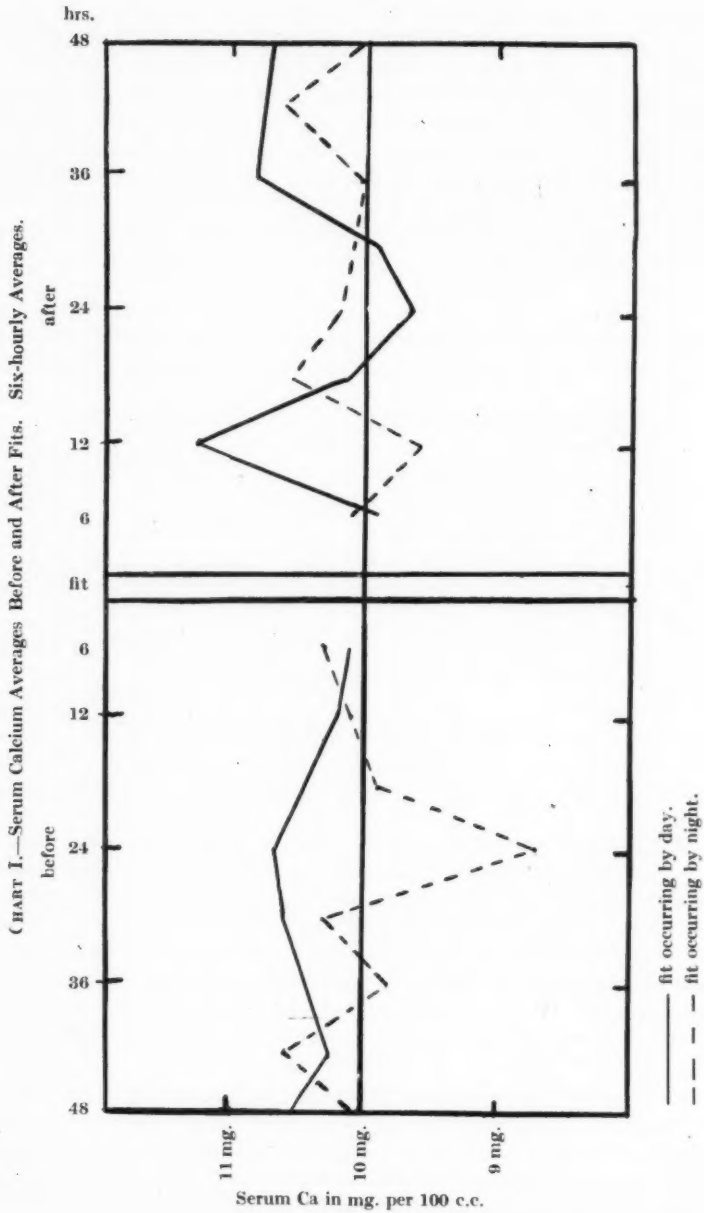


CHART I.—Serum Calcium Averages Before and After Fits. Six-hourly Averages.

The influence of the drugs taken as routine treatment was noted. There is not much difference, but the group having luminal showed slightly higher average values than those who were not on this drug.

TABLE V. INFLUENCE OF DRUGS ON CALCIUM CONTENT

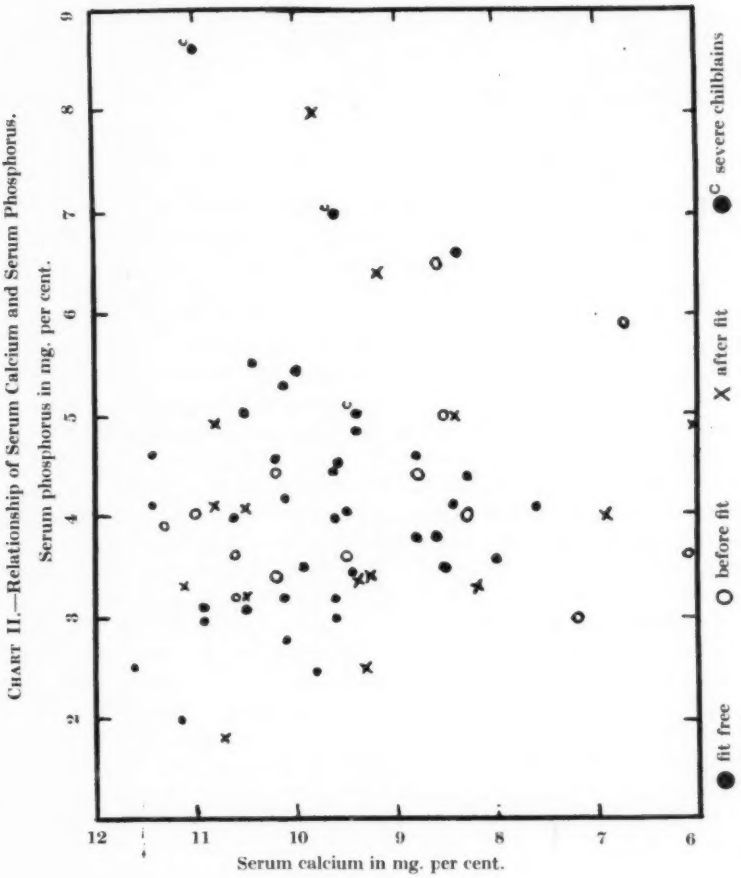
On luminal	15 cases	average Ca 10·16 mg.
bromide	8	9·98
luminal and bromide	9	10·01
other drugs	10	10·07

The effect of intensive calcium treatment, and of diminution of the serum calcium, was studied in certain cases. Eight patients who tended to have a low calcium level were given one drachm of calcium gluconate by mouth three times a day, two drachms of cod liver oil and a pint of milk daily, in addition to their normal diet, for a period of four months or more. Of these, five showed an increased level of serum calcium, which, however, was erratic and ill-sustained. In two cases there was a slight increase of fit incidence, in two there was no change, and in the other there was some degree of improvement. In two of these cases an increase of fits followed the cessation of the calcium treatment. In one of the cases the improvement was very marked. This patient had for many years had repeated and severe attacks of status epilepticus as well as isolated fits. During the three years preceding the investigation he had had 22, 15 and 19 status attacks respectively, and during the first three months of 1932, 10 attacks. Calcium gluconate intravenously had been given in four of these, with immediate results on two occasions. In April, 1932, he was put on the calcium régime. Since then there have been only five status attacks during 20 months, though there has been no reduction of the isolated fits. Another patient was started on calcium treatment after an attack of acute tetany. Blood taken during the attack, which was stopped by intravenous calcium, showed a serum calcium value of 10·7 mg., but subsequently he had on several occasions lower values of 7·7 to 8·4 mg., unconnected with fits. In fact, for six months he had no fits, though this should probably be attributed to luminal rather than calcium.

Five patients who tended to have a high calcium level were given sodium sesquiphosphate in doses of 10 grains three times a day. In three cases the calcium level was markedly reduced, while in all the cases there was an increase in the number of fits, the increase being persistent for two or three months after stopping the treatment. It appears, therefore, that while increase of calcium is not in itself sufficient to control the fits, a diminution of calcium is definitely detrimental.

SERUM PHOSPHORUS

On 70 occasions the serum phosphorus and calcium were estimated on the same sample of blood. For this purpose the blood was spun immediately, and the serum calcium values may therefore be inaccurate, though the



calcium phosphorus ratios obtained suggest that the error is not great. The average value obtained for phosphorus was 4·493 mg. per 100 c.cm., while the average calcium was 9·23 mg., rather lower than the average obtained when the clot is left overnight. The range for the phosphorus readings was from 1·8 to 11·4 mg.; in 46 cases it lay between 3 and 5 mg.

TABLE VI. CORRELATION OF PHOSPHORUS WITH MAJOR FITS

Fit-free interval	38 cases	average 4·31 mg.
Within 48 hours before fit	16	4·12
,, ,, after	10	4·36
Between two fits, within 48 hours of either	6	3·73

These values for serum phosphorus agree with the findings for serum calcium shown earlier, the lower phosphorus before fits corresponding with the higher calcium, and vice versâ.

The relationship between phosphorus and calcium does not seem to be consistently disturbed in connection with epileptic fits, as shown in the 'scatter' diagram (Chart II). Though most of the values outside the normal area (3 to 5 mg. phosphorus and 9 to 11 mg. calcium) are related to fits or to severe chilblains, an equal number of values within 48 hours of a seizure are within the normal.

SUMMARY

1. In a series of observations over a period of time on a limited number of cases, the average serum calcium is found to fall within normal limits, though the range of values is wide and variable, for the group and for individuals alike.

2. The average of values before a fit is found to be greater than that after a fit. The highest range of values is that obtained during a run of fits, while low values are found after a run. In two cases, estimations made during a run of fits which terminated fatally proved to have definitely low values.

3. When cases of fits by day are contrasted with those of fits by night, the averaged figures show that the behaviour of the serum calcium in relation to the attacks varies inversely in the two groups. This inversion is confirmed in a striking manner in one particular case, which gives low values after day fits, high values after night fits, and a persistent median value in fit-free intervals.

4. Treatment with large doses of calcium may have beneficial results, while the diminution of serum calcium by sesquiphosphates is definitely detrimental.

5. Serum phosphorus is found to be within normal limits, though with a wide range of variation. Its relation to the serum calcium is not always disturbed by fits, though abnormal ratios may be associated with attacks.

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CHOLESTEROL TUMOUR (CRANIOPHARYNGIOMA) OF THE PITUITARY BODY

By

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CLINICAL CASE

THE patient, when 47 years of age, was shown by one of us (F. P. W.), in May, 1927, at the Clinical Section of the Royal Society of Medicine with the diagnosis 'Pituitary (cystic ?) Tumour.' [1] He had then a pale, cachectic appearance, with somewhat wizened, shrivelled face; moderate anæmia; more or less chronic headache, especially in the upper occipital region; bilateral temporal hemianopia and, on radiographic examination, considerable anteroposterior enlargement of the pituitary fossa. A negative Wassermann reaction was obtained in both blood serum and cerebrospinal fluid, and the latter was normal in all other respects. There was no polyuria. Blood-sugar (May 17, 1927) was 0·082 per cent. The blood-sugar curve was not abnormal. The blood pressure was 126 mm. Hg. systolic; 88 mm. Hg. diastolic. The patient had no axillary hair and only scanty hair on pubes, eyebrows and face, and he stated that he never had had any more than this. The testicles were rather small. He had four children, all living and healthy, but had been sexually impotent for the past year.

He dated his symptoms from an attack of influenza about February, 1925, and in the summer and autumn of that year had been found already to have anæmia, headache, bilateral temporal hemianopia and enlargement of the pituitary fossa. Later, in February, 1926, there had been some improvement. Afterwards he progressed fairly well and was able to continue his work as dock clerk until his fatal illness of September, 1933.

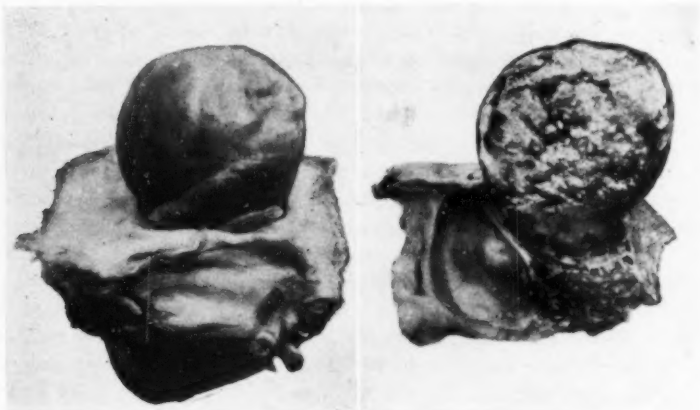
A radiogram of the sella turcica region taken in September, 1933, showed the dorsum sellæ indistinct and the pituitary fossa enlarged, apparently measuring 12 mm. in length and 11 mm. in depth.

He died from an acute diarrhœal febrile disease. Morgan's bacillus was cultivated from the fæces and his blood-serum gave a positive agglutination reaction for the dysentery bacillus of Sonne, but this latter reaction may have been due to a past dysenteric infection.

PATHOLOGICAL EXAMINATION

At autopsy (September 30, 1933), a globular tumour was seen projecting from the position of the pituitary fossa (fig. 1, *a*). Its appearance suggested that of a small round chestnut with a comparatively smooth

external surface, brownish in general colour, but with mottled darker brown patches of old hæmorrhage just beneath the surface; and a thin elastic crackly parchment- or shell-like capsule, fibrous and with some slight calcification. The compressed optic nerves passed obliquely forwards from beneath each side of the tumour, while further back the middle cerebral artery was seen passing forwards, outwards and upwards. The measurements of the mass were: anteroposterior diameter, 30 mm.; transverse, 28 mm.; vertical, 30 mm.—i.e. it was almost an exact sphere. The anteroposterior measurement of the shallow pituitary fossa was 23 mm. from the situation of the slight



(*a*) (*b*)

FIG. 1.—Naked-eye photographs of tumour after removal. (*a*) Right lateral aspect (illustration 2 mm. smaller than actual size) shows the general appearance of the tumour projecting upwards from the sella. The right optic nerve and middle cerebral artery are seen passing obliquely forwards and upwards. (*b*) Mesial sagittal section (actual size) shows the crumbling cholesteatomatous contents of the cyst and the subcapsular hæmorrhages, the shallow eroded sella with the compressed remains of the pituitary body on its floor and the sphenoidal sinus in the body of the bone.

prominences representing the flattened-out remains of the almost completely destroyed clinoid processes.

On median vertical section, the mass was found to consist of crumbling, loose, semi-necrotic rather dry-looking granular to slightly soapy débris, mixed with innumerable fine cholesterol crystals glistening like frost (fig. 1, *b*). Here and there towards the periphery there was a small amount of firmer pearly-white fibrous tissue shading off into the softer and more central material, evidently largely amorphous or necrotic. There were several red to brownish subcapsular hæmorrhages of varying ages to which the mottled appearance of the outside of the tumour was due. The sella was enlarged, eroded and shallow, its saucer-like concavity being occupied by a thin layer of more or

less degenerated or necrotic-looking tissue, rapidly shading off above into the general contents of the cyst ; the whole section was rather reminiscent of the shape of a ' button mushroom ' with a wide stalk attached below to the shallow floor of the sella and with its interior undergoing decay.

MICROSCOPICAL EXAMINATION

Fresh wet films of the contents of the cyst showed a mixture of granular débris with numerous typical crystalline plates of cholesterol, together with

FIG. 2.—A low-power photograph of the compressed pituitary glandular tissue, stripped from the floor of the sella, the whole thickness of which is included in a single low-power field. The glandular acini are compressed and atrophied, with an increase of connective tissue between them. Some of the cholesterol-clefts are shown at the upper part of the photograph, and it will be noted that there is no irritative cellular reaction around them, unless there is some other cause of this, such as hæmorrhage or inflammation. No squamous epithelial cells have survived in this area. Hæmatoxylin and eosin. × 200 diam.

the disintegrating remains of a few cells, the nature of which in these preparations was now unrecognisable, and red blood corpuscles both hæmolysed and fresh.

Sections in continuity were somewhat difficult to obtain, owing to the crumbling nature of the specimen. In the intrasellar or basal portion, there was, at the margin, a thin compressed layer of much degenerated pituitary glandular tissue, the surviving cells being chiefly eosinophil with only an occasional basophil cell (see figs. 2 and 3) mixed with proliferated connective tissue of varying density. Internal to (i.e. above) this were the contents of the cyst, which were composed of much granular and amorphous débris

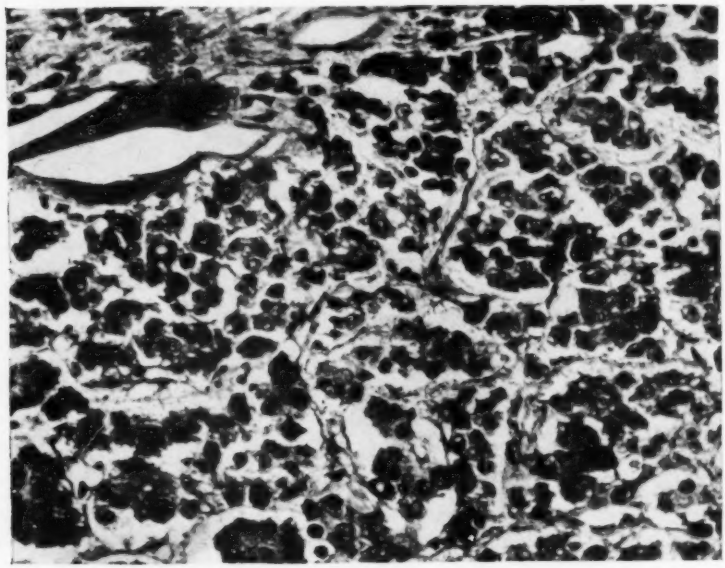


FIG. 3.—High-power photograph of an area of surviving pituitary glandular cells from the floor of the sella. Some cholesterol-clefts are seen at the upper left corner, with some degenerated remnants of squamous epithelium around them (compare with next figure), this part of the section corresponding with the capsule covering the upper surface of the gland. The surviving cells in the plane of this mesial section are predominantly eosinophil. There is rather less fibrosis in this particular area than in some other parts. Hæmatoxylin and eosin. × 400 diam.

together with old degenerated and hyaline connective-tissue trabeculæ (the latter most continuous and distinct towards the periphery), between and amongst which were very numerous cholesterol-clefts of varying size lying at all angles to one another (fig. 4). Around most of these clefts there was no irritative cellular reaction, their immediate surroundings being either dense, almost non-cellular fibrous tissue, or non-cellular amorphous and structureless degenerative material. Here and there, but practically only towards the periphery, in or just under the connective-tissue capsule, the faint outlines of degenerated cells could be made out; there were also numerous hæmor-

rhages, both recent and old. It was only in, or in the immediate neighbourhood of, these hæmorrhagic areas that such cells were found. The latter were mostly 'foam-cells' as well as other varieties of phagocytic tissue- and wandering cell, but with only an occasional polymorph (i.e. there was no suppurative reaction), together with some scanty collections of small round and plasma-cells, and also some young connective-tissue cells—again mostly in areas where there was a considerable amount of blood-pigment; probably these represented a chronic irritative phenomenon accompanying and following upon the hæmorrhage. No squamous epithelium or any adamantinoma-

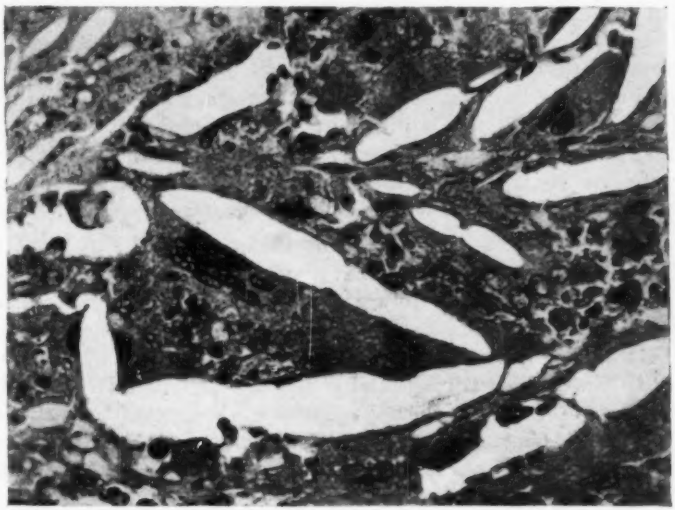


FIG. 4.—High-power photograph of some of the cholesterol-clefts just beneath the fibrous capsule. Round some of these are seen the last surviving squamous epithelial cells from which the tumour originated. These cells tend to become plasmodial and multinucleated as they degenerate. All stages of this process can often be traced in similar cases, but in the present instance only these extremely scanty and much degenerated cells were found in many sections examined. Van Gieson and hæmatoxylin. × 500 diam.

tous tissue could be detected throughout the main mass of the tumour, but very occasionally, around some of the cholesterol-clefts towards the periphery, there were a few irregular and degenerated large plasmodial cells (fig. 4) which appeared to be the last remaining survivors of the squamous epithelium from which this cystic tumour had evidently originated, i.e. the tumour was a squamous-celled suprapituitary craniopharyngioma or hypophyseal-duct tumour. It had arisen from squamous remnants of the duct, which had persisted in one of the common sites for such remnants, viz. in the capsule covering the upper surface of the pituitary gland. Another common site is the anterior surface of the infundibulum.

The domed 'roof' or capsule of the tumour consisted of dense, rather hyaline fibrous tissue, mostly comparatively non-cellular except in and around the hæmorrhagic areas, and, as already noted, with only the minimal remains of any squamous epithelium here and there in the deeper part of the capsule. In the superficial layer of the latter were abundant patches of finely granular dark golden-brown blood-pigment, which gave the typical Prussian blue reaction of hæmosiderin—mostly free in the tissue spaces, but, near the more recent hæmorrhages, still contained within mononuclear phagocytes.

SUMMARY

The tumour is, therefore, a very old-standing (congenital) squamous-celled craniopharyngiomatous or hypophyseal-duct cyst which has become cholesteatomatous with almost complete disappearance, by a process of 'natural cure,' of the squamous cells from which it originated. In other words, it is not a Rathke's pouch or intraglandular-cleft tumour. The pituitary gland itself has undergone very extensive pressure atrophy, the thin layer of surviving glandular cells—at all events in the mesial plane represented in the sections examined—being predominantly eosinophil.

COMMENTARY

The group of craniopharyngiomas comprises all the squamous epithelial intracranial growths of the pituitary region, both cysts and solid formations. Thus the lesions variously termed hypophyseal-duct tumours, suprasellar cysts, Rathke's pouch tumours, ameloblastomas and adamantinomas are all included. Their origin is congenital and, although symptoms may develop at any age from the first to the seventh decade, they most frequently appear in childhood and adolescence. The modified cubical-celled epithelium, which at first lines the hypophyseal duct, normally disappears, but from its remnants may develop squamous epithelial tumours. These develop from the anterior surface of the infundibulum (suprasellar or supradiaphragmatic craniopharyngioma) or, as in the present case, from beneath the capsule covering the anterior pituitary lobe (intrasellar or subdiaphragmatic craniopharyngioma). In the latter form, the pituitary body is compressed; its remains are usually found in flattened crescentic form in some part of the floor of the sella. It is frequent to find these remains only on microscopical examination.

Among 80 cases of craniopharyngioma analysed by Cushing,[2] in only seven did the first symptoms appear in the fifth decade. The age-distribution in the series was as follows:—

1st	decade	.	.	15	cases
2nd	,,	.	.	27	,,
3rd	,,	.	.	15	,,
4th	,,	.	.	10	,,
5th	,,	.	.	7	,,
6th	,,	.	.	4	,,
7th	,,	.	.	2	,,

In the younger cases interference with the normal secretory activity of the anterior pituitary lobe is from the outset usually manifest by retarded growth and imperfect genital development. Obesity is also frequent. When symptomatic evidence of the lesion is postponed until the fourth decade or later, growth and development may have been normal; the initial symptom is then usually some visual disturbance, e.g. hemianopia or papillœdema. As in the case we record, it is not infrequent at this age for the patient to present a pale and cachectic appearance with wrinkled skin and reduced bodily hair. Impotence is the rule, and polyuria is very frequent; this latter symptom was not present in our patient. The blood-pressure is often very low, even in adults. Cushing records a systolic pressure of 60 mm. (diastolic 50 mm.) in a patient aged 23, and 80–90 mm. systolic is not infrequent.

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THE pH AND LACTIC ACID CONTENT OF THE CEREBROSPINAL FLUID

By

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Recently we have been engaged in an investigation in regard to the relationship of blood pH to that of tissue. Spinal fluid was used as tissue for the purpose of this inquiry. Our observations proved that the current teaching according to which the spinal fluid is more alkaline than blood is erroneous. We believe that our figures are reliable because we employed a method for the determination of pH which is superior to those available to previous workers in the same field.

The majority of authors give pH reading of cerebrospinal fluid in normal cases without referring at all to the acid base balance in the blood. The majority of figures recorded are rather on the high side. Weston [1] gives it as 7·9–8·3; Felton, Hussey and Bayne-Jones,[2] 7·7–7·9; Vogt,[3] 7·4–7·6; Shearer and Parsons,[4] 7·3–7·4; Levinson,[5] 7·4–7·6; Eskuchen and Lickint,[6] 7·36–7·5; Beaumont and Dodds,[7] 7·45.

Cameron and Gilmour [8] give expression to the current teaching by stating that the pH of the spinal fluid is slightly more alkaline than that of the blood. McQuarrie,[9] however, believes that within the limits of experimental error the pH of spinal fluid always approximates to that of the blood. Cernatescu and Mayer [10] apparently were the first to observe greater acidity in the spinal fluid than in the blood. The figures given by these authors for spinal fluid are extremely low. They use, however, the Quin-hydrone electrode—an electrode which is unreliable for fluid containing protein.[11] Previous to their work, however, Parsons and Shearer concluded that cerebrospinal fluid is more alkaline than blood only at a low carbon dioxide tension.

There is no doubt that in many instances the high pH readings were due to the employment of methods which disregarded the CO_2 loss of the fluid, and other erroneous conclusions have been arrived at owing to disregard of the temperature factor. So far as we are aware, none of these investigators used the glass electrode.

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METHOD

The glass electrode was employed and was adapted for the use of blood and spinal fluid. As is generally recognized, it is superior not only to the colorimetric but also to other electrometric methods. There are two main difficulties with these methods so far as cerebrospinal fluid is concerned. It is not possible to use paraffin for the purpose of avoiding CO_2 loss, since the contact of paraffin with the glass membrane fouls the electrode. The other difficulty is that of temperature. If determination is made in room temperature a correction factor has to be used which is variously given by different authors. In addition it is essential for various reasons to make determinations in the shortest possible time. In such circumstances it would be difficult to be sure that a proper equilibrium between fluid and buffer solution has been established. To avoid the difficulty the whole investigation was made in a room heated to body temperature. To avoid CO_2 loss the method used was as follows : The ordinary canula in use for cerebrospinal work was employed. Connected to it was a piece of fine rubber tubing of a narrow bore, about 3 inches in length. The distal end of the tubing was inserted in the inner chamber of the electrode. This chamber fills up with fluid and overflows, so that the fluid whose pH was taken never came in contact with air. A detailed account of this method will be found in the *Journal of Physiology* (1934, vol. 81, p. 197).

Twelve cases were investigated altogether. They were all in-patients of the Heart Hospital. The majority of these patients did not exhibit any evidence of heart failure, and from the point of view of composition of the blood and the spinal fluid they must be considered as normal cases. There were, however, cases which exhibited definite evidence of heart failure. One case suffered from pronounced hyperthyroidism. These patients had been mostly resting in bed for a considerable time. However, a few minutes before the specimen of the spinal fluid was taken they were subjected to a slight exertion. They were taken from the wards by a wheel-chair and transported by means of a lift to two flights of stairs below, where they had to walk a few yards to a couch. It seems unlikely that there could have been an appreciable rise in the lactic acid of blood as a result of this exertion, so far as the great majority of cases were concerned.

Table I shows that only once did the pH exceed 7·4—all the others were below this figure. It will also be seen that there is a definite relation between the pH of spinal fluid and that of blood, and that the latter is more on the alkaline side than the former. Incidentally, it shows that it is impossible to establish absolute values for pH of spinal fluid unless the acid balance of the blood is also determined. As is to be expected, there is no relationship between lactic acid and pH reading.

An explanation why the cerebrospinal fluid is more acid than blood may be found in the difference of behaviour of CO_2 in these two fluids.

TABLE I

Case	Sex	Age	pH	
			Blood	C.S.F.
1	M	20	7·45	7·41
2	M	25	7·42	7·35
3	M	50	7·42	7·37
4	M	53	7·39	7·35
5	F	39	7·42	7·39
6	M	47	7·39	7·37
7	F	67	7·44	7·37
8	F	69	7·46	7·39
9	F	23	7·42	7·34
10	F	54	7·43	7·36
11	M	55	7·40	7·30
12	F	47	7·42	7·37
	Average readings:		7·42	7·36

Parsons and Shearer have shown that 'the reaction changes occurring in spinal fluid with increasing carbon dioxide tension are much more pronounced than those occurring in normal blood.'

LACTIC ACID

It appears again that the findings of different investigators in regard to lactic acid in cerebrospinal fluid are variable. Greenfield and Carmichael [12] state that lactic acid is normally absent from cerebrospinal fluid, or present only in minute traces. Cameron and Gilmour, in discussing the relative concentration of the constituents of human blood plasma and cerebrospinal fluid, do not mention the presence of lactic acid. De Sanctis, Killian and Garcia [13] state that the normal lactic acid content of blood is 16 to 22 mg. per cent., and that the fluid figure is about 75 per cent. of that of blood.

Wittgenstein and Gaedertz [14] investigated the relations between blood lactic acid and that of spinal fluid in animals and man, and they found that at rest the lactic acid contents of the blood and cerebrospinal fluid were approximately equal—plasma at rest, 15 to 18 mg. per cent., cerebrospinal fluid at rest, 13 to 16 mg. per cent. In cases where the lactic acid is low, blood plasma and cerebrospinal fluid equal each other. Where lactic acid increases in the blood it also increases in the spinal fluid.

Zweifel and Scheller [15] state that lactic acid disappears more slowly in the cerebrospinal fluid than in the blood, and they also assume that the acid rises more slowly in the fluid.

METHOD

The estimation of lactic acid in blood and fluid was carried out by the iodometric method introduced by Clausen [16] and modified by Friedemann, Cotonio and Shaffer,[17] and later by Friedemann and Kendall.[18] The principle of the method is the formation of acetaldehyde from lactic acid when the latter is oxidised by heating with potassium permanganate. The aldehyde is collected, by a process of aeration, into sodium bisulphite solution, and titrated by Clausen's method.

The protein was removed from the blood by the Folin-Wu method, while sugar and other interfering substances were precipitated by means of the Van Slyke [19] copper-lime treatment. In the case of spinal fluid, protein precipitation was carried out according to the modification of the Folin-Wu technique suggested by Beaumont and Dodds,[20] while the sugar was dealt with as in the case of blood. Application of the old and new protein precipitation methods to spinal fluid showed no significant difference as far as the lactic acid content is concerned.

All the estimations were commenced almost immediately after the removal of the blood or fluid, so as to ensure that no extra lactic acid was

TABLE II

Case	Sex	Age	Lactic Acid		Diagnosis
			Blood	C.S.F.	
1	M	20	37	Not done	Aortic regurgitation, mitral stenosis
2	M	25	38	37	Auricular fibrillation, congestive failure
3	M	50	33·5	32·5	Aortic regurgitation, mitral stenosis, auricular fibrillation
4	M	53	37	22	Partial heart block
5	F	39	24	25·5	Mitral stenosis, slow fibrillation
6	M	47	26	26	Angina of effort
7	F	67	33·5	35·5	Hyperpiesia
8	F	69	59	45	Hyperthyroidism, high blood pressure, congestive failure
9	F	23	31·5	31·5	Mitral stenosis, auricular fibrillation
10	F	54	26	24	Hyperpiesia, angina pectoris
11	M	55	35	36·5	Angina pectoris
12	F	47	33	28	Mitral stenosis, aortic stenosis
Average readings:			34·5	31·2	

formed by autoglycolysis of the sugar present. Double estimations were carried out on nearly every specimen of blood and fluid.

Here again (Table II), it is clear that the lactic acid content of the spinal fluid stands in definite relation to that of the blood. It must be kept in mind in analysing the table that the method of determining lactic acid has a maximum margin of error of, say, + 5 per cent. — 5 per cent.

In six cases out of eleven the lactic acid content of the spinal fluid was lower than that of blood; in three cases it was higher. In the latter the difference in the lactic acid content of the two fluids was so small as to come within the limits of the margin of experimental error. On the other hand, in some instances the lactic acid content of the fluid was so definitely below that of the blood that the difference between the two fluids in this respect cannot be accounted for by any experimental error. We may safely assume therefore that there are cases where the lactic acid content in the fluid is definitely lower than that in the blood. We may assume that if the patient is completely at rest for a considerable time an equilibrium between these two fluids will approximately be established. However, if lactic acid is being actively formed in the organism one of two things may happen. As long as the lactic acid blood level continues to rise this level may be higher than that of the fluid, because the latter can only increase its lactic acid store by a process of relatively slow diffusion from the blood. On the other hand, lactic acid disappears from the blood at a much quicker rate than does the acid from the spinal fluid. It is therefore possible that immediately after exercise there may be a higher percentage of lactic acid in the spinal fluid than in the blood. The difference in level between the lactic acid content of blood and spinal fluid in the case of exophthalmic heart failure is easily explained. We know that in such cases the oxygen consumption is very high and the oxygen 'debt' also high, which means a high level of blood lactic acid. Moreover, as this patient suffered from pronounced heart failure it is likely that a slight exertion was sufficient to raise the lactic acid level to a considerable degree. For reasons stated before, the lactic acid level in the spinal fluid would rise in such circumstances but slowly. However, the pronounced difference of lactic acid content of blood and fluid in the case of the patient suffering from partial heart block is less easily explicable on these grounds. It is true the patient had suffered from degenerative myocarditis, but the lactic acid in the blood is apparently within normal limits.

The figures also suggest that in heart failure the lactic acid level in blood and fluid is raised, as was to be expected.

CONCLUSIONS

(1) The pH of the cerebrospinal fluid is lower than that of blood.

(2) The lactic acid contents of cerebrospinal fluid and blood are approximately the same, provided sufficient time is allowed for an equilibrium between the two fluids to be established.

We wish to express our indebtedness to Mr. Shutt, Lecturer in Chemistry in the University of Liverpool, for valuable help given in this investigation.

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APPENDIX

Cases—Brief Summary

(1) McMerryman. Substernal pain and flatulence with palpitation—6 months. Aortic regurgitation and mitral stenosis. B.P. 140/75. No congestive failure.

(2) Hamilton. Dyspnœa and exhaustion—2 months. Rheumatic fever 1904. Mitral stenosis and aortic regurgitation. Auricular fibrillation—rate 70. B.P. 120/75. No congestive failure.

(3) Blower. Dyspnœa on exertion—3 years. Heart of normal size. Rate 55. B.P. 140/60. E.C.G. Partial heart block. No congestive failure.

(4) Smith, M. Dyspnœa and palpitation—6 months. Mitral stenosis. Auricular fibrillation. Rate 60 ? Block ? Digitalis effect. B.P. 130/ ? No congestive failure.

(5) Downey. Typical angina of effort. Fundamental rhythm normal. B.P. 140/85. No objective signs of failure.

(6) Arrowsmith. Breathlessness and palpitation after exercise—5 years. Rheumatic fever 1923. Mitral stenosis. Auricular fibrillation. Rate 80. B.P. 110/ ? No evidence of congestive failure.

(7) Flynn. Cardiac pain of anginal distribution and dyspnœa—9 months. Tic-tac rhythm. Rate 80. B.P. 125/80. Arteriosclerosis and emphysema. No œdema.

(8) Sanderson. Five years' history of dyspnœa on exertion. Scarlet fever in youth. Mitral and aortic stenosis. B.P. 135/80. Rate 90. Liver and spleen not felt. No ascites. No œdema of legs.

(9) HANNAKIN. Exhaustion, dyspnœa and swelling of feet—6 months. Auricular fibrillation. Rate 90. B.P. 125/? 60. No gross valvular lesion. Slight œdema of legs. Liver enlarged 2 inches below costal margin.

(10) COULTON. Dyspnœa on exertion and substernal pain—2 months. Swelling of left lobe of thyroid—30 years. Typical thyrotoxicosis. Fundamental rhythm normal. Rate 110. B.P. 230/80. Some œdema of both legs.

(11) FLETCHER. Dyspnœa—slight at rest but marked on exertion—3 years. Rheumatic fever at 12. Scarlet fever and generalized œdema at 14. Normal rhythm. Rate 75. B.P. 200/100. No congestive failure.

(12) CULLIGAN. Giddiness and precordial pain of anginal type—4 years. Normal rhythm. Rate 74. B.P. 200/100. No gross arteriosclerosis. No congestive failure.

COLLOID CYST OF THE THIRD VENTRICLE ASSOCIATED WITH CONGENITAL CYSTIC KIDNEYS *

By

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WHILE true neoplasms in the region of the third ventricle are of fairly common occurrence, colloid cysts within its cavity are somewhat infrequently met with. The first two cases in this country were published by Batten and Collier (1899) and Mott and Barratt (1899); these were followed by Kinnier Wilson's case in 1906. The first series of cases was collected by Hall (1913), who found seven cases in the literature and added two of his own. Twenty years later, Zimmerman and German (1933) reviewed all the recorded cases, 28 in number, and added two more, one of which was successfully operated on. Dandy (1934), in his recent book on benign tumours of this area, records operations on five cases of colloid cyst. The cyst wall was removed completely in all and there was only one fatality—a month after the operation—due to blocking of the aqueduct of Sylvius. Cysts in this region are not always of choroid plexus or ependymal origin. In a number of reported cases they have been epidermoid or parasitic in nature; others are stated to be derived from the hypophysis. One case was considered by the author to be a degenerated sarcoma—myxosarcoma, while other cases appear to have been cystic dilatations of the cavum septi pellucidi—a condition that has been described by Dandy (1931). Byrom and Russell (1932) considered that of all the reported cysts in this region only 20 were of the ependymal or choroid plexus type, and that some of these were inadequately described histologically.

The following case is recorded because of the rarity of colloid cysts of the third ventricle, the difficulty of diagnosis and the association of the condition with congenital cystic disease of the kidneys. It is not proposed to review the literature on the subject, as this has been done recently by Zimmerman and German. Tumours in the region of the third ventricle have been extensively dealt with by Fulton and Bailey (1929), who include a case of colloid cyst in their series. Both of these articles are accompanied by a comprehensive bibliography.

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REPORT OF PERSONAL CASE

Clinical Findings.—The patient, a schoolboy, age 16, was referred to one of us by Dr. R. G. McWhinney after two days' illness. His previous history contained nothing relevant apart from the history of a slight knock on the head two days prior to admission. He had always been a healthy boy and the family history was clear.

It was stated by his parents that he was perfectly well until about 48 hours before coming to the hospital. He then began to complain of severe headache, which failed to respond to the usual remedies. Within a few hours nausea was complained of, and vomiting soon became a troublesome feature. By the following day he was stuporose, and his attention was only attracted with difficulty.

When admitted to hospital the next day, the patient was comatose, but he resented actively the process of examination. His attitude was that of cerebral irritation, and a moderate degree of photophobia was present. Although of rather slight build, he was of average muscular development, and early secondary sexual characteristics had appeared. The pulse rate was 60 per minute, and the temperature was 97° F.; breathing was quiet and the respiratory rate was 24. There was no rash, cyanosis, anæmia, clubbing of the fingers or jaundice. Proptosis and exophthalmos were not observed.

Adequate neurological examination was impossible owing to complete lack of cooperation on the part of the patient. Slight bilateral papillœdema was found. There were no retinal hæmorrhages or exudates. The pupils were somewhat dilated and their reaction to light was sluggish: there was some degree of paralysis of associated ocular movement, but the attempt to analyse it was not very satisfactory. The main ocular paresis appeared to affect both internal recti. There was no weakness of the external recti. The corneal reflexes were present and equal. The usual test for cerebellar dysfunction could not be carried out. The limbs were neither spastic nor hypotonic, while the knee and ankle jerks were sluggish and the plantar responses were bilaterally extensor. Kernig's and Brudzinski's signs were negative, and there was no head retraction. There seemed to be a generalized hyperalgesia. Clinical examination revealed no gross abnormality of the heart and lungs. The lower pole of the right kidney was easily palpable; the liver, spleen and left kidney were not felt. The patient had urinary incontinence, and on catheterization only a few cubic centimetres of urine were obtained. This was found to be loaded with albumin, but no sugar or acetone was present.

A tentative diagnosis of subarachnoid hæmorrhage was made. Lumbar puncture revealed spinal fluid under increased tension. Manometric reading was not taken owing to the restlessness of the patient. A small quantity of fluid was withdrawn, and it was neither xanthochromic nor turbid. A fibrinous clot did not form on standing. At this stage it was considered that the patient had an intracranial tumour, but its situation was not localized. The boy's condition became rapidly worse and death occurred within three hours of admission.

On examination, the cerebrospinal fluid was clear and contained a normal amount of protein, and 28 cells (mostly lymphocytes) per c.mm. were present. The chloride content was 718 mg. per cent., and the Wassermann reaction was negative.

PATHOLOGICAL FINDINGS

Autopsy (24.5.34).—The body was that of a well-nourished adolescent male.

Brain.—The brain appeared large and œdematous, and there was an excess of clear cerebrospinal fluid at the base. There was no evidence of

meningitis nor were there any hæmorrhages. Both lateral ventricles were distended with clear fluid and dilated. Almost filling the third ventricle and attached to the choroid plexus of the velum interpositum was a spherical thin-walled cyst, 1·5 cm. in diameter. The cyst was hanging freely in the third ventricle, but on its superior aspect possessed a vascular point of attachment to the anterior end of the velum interpositum. The third ventricle itself appeared somewhat dilated.

Kidneys.—The right kidney weighed 9 oz., the left 8 oz. Both kidneys showed a polycystic condition. The cysts were not apparent on examining the surface of the kidneys, but on the opening of each organ multiple small cysts were found lying deeply within the cortex, and mainly at or near the junction of cortex with medulla. The largest single cyst was not more than 4 mm. across, and the smallest cysts were of pinhead size. In areas, a group of small cysts formed a honeycomb nodule about 1·5 cm. in diameter. The capsules of the kidneys stripped with ease, and no other changes were seen.

Other organs were carefully searched for cystic disease, but none was found.

Lungs.—An active caseating tuberculous focus was found at the base of the left upper lobe, and a small fibrous nodule was present in the left lower lobe. The left hilar glands were enlarged and showed commencing caseation.

MICROSCOPICAL EXAMINATION

Third Ventricle Cyst.—The contents of the cyst, which, in the fresh specimen, were of a viscid fluid nature and turbid, became brittle with fixation. Under the microscope, the cyst was seen to be filled with a homogeneous eosinophilic material. A few cuboidal epithelial cells and an occasional leucocyte were scattered throughout this hyaloid matrix.

The cyst wall was constructed of thin connective tissue, on the inner surface of which was a lining of epithelium. At one point on the circumference the connective tissue wall became thicker and highly vascular and merged insensibly with the vascular stroma of the choroid plexus (fig. 1). At this point the outer wall of the cyst was in relation to choroid plexus, but elsewhere on the outer surface—that bathed by the fluid in the third ventricle —there was an incomplete much-flattened epithelium, the nature of which it was impossible to determine. The lining epithelium of the cyst consisted of cuboidal cells with round dark nuclei identical with choroid plexus epithelium (fig. 2). These cells were arranged in a single layer round most of the circumference, but at the point of attachment to the choroid plexus the lining epithelium of the cyst became four to six layers deep, although neither invasion of the stroma nor papillomatous formation occurred. These cells did not appear to possess cilia.

Sections were stained by Cajal's gold-sublimate method, and the connective tissue of the cyst wall was determined to contain a few well-developed astrocytes.

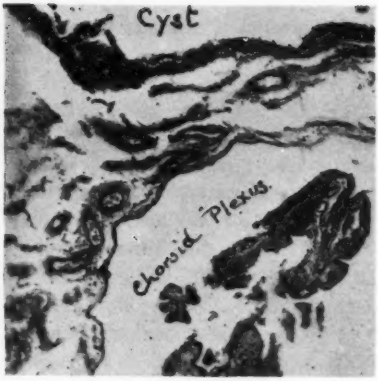

FIG. 1.—Wall of cyst of third ventricle at the point of attachment to the choroid plexus. At this site the lining epithelium of the cyst is four to six layers in depth. × 48.

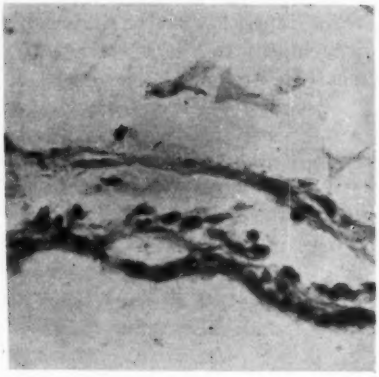

FIG. 2.—Wall of cyst of third ventricle, showing single layer of non-ciliated cuboidal epithelium. × 440.

FIG. 3.—Section of kidney. The cyst here shown is lined by a single regular layer of cells identical with the epithelium of the renal tubules. × 440.

Kidneys.—The cysts in the kidneys presented the varying features frequently met with in polycystic disease, though the small size of the cysts and the lack of general involvement of renal tissue were unusual. Some of the cysts were lined by a single regular layer of short columnar cells indistinguishable from renal tubule epithelium (fig. 3). Other cysts had a lining of shorter, cuboidal cells, and others a simple flattened epithelium, closely applied to an encircling stroma of connective tissue. A considerable formation of fibrous tissue was apparent around the larger cysts.

Lungs and Bronchial Glands.—The presence of active tuberculosis was confirmed.

DISCUSSION

Clinical.—Diagnosis of third ventricle cysts is, as yet, rarely possible during life, though Zimmerman and German localized the lesion in their cases and the nature of the obstruction was revealed at operation. They lay great emphasis on the localizing value of ventriculography in the investigation of the cases. Many of the patients have been young, half being under thirty-five years of age, and the present case is the youngest recorded. A number of patients have died suddenly, some being found dead; others were found unconscious and died within a few hours. These cases are, therefore, of medicolegal as well as pathological interest. Drennan's cases (1929) were both the subjects of coroners' inquests.

The symptoms and signs of this condition naturally fall into two groups: (*a*) generalized increased intracranial tension, and (*b*) localizing factors. When the patient is comatose it is likely that the features of the first group will be mostly in evidence. Headache, vomiting, mental dulness, apathy, coma and papilloedema were the principal manifestations of increased intracranial pressure in this case, and it is doubtful whether the bilateral extensor plantar responses and urinary incontinence were of any localizing value. The onset of acute hydrocephalus in these cases is due to sudden occlusion of the foramina of Munro or the aqueduct of Sylvius by the cyst. It is possible that the slight blow on the head which our patient sustained just prior to the onset of his headache was sufficient to cause a displacement of the cyst and so lead to the development of hydrocephalus. The occlusion is not always permanent; if it is only temporary and intermittent the symptoms will vary accordingly. In a number of cases it is stated that moving the head in certain directions relieved the severe headaches, the relief being often sudden and striking. This phenomenon, though suggestive of a ball-valve action of a cyst in the third ventricle, is not always diagnostic, as it may occur with tumours of the posterior fossa. Attacks of hypersomnia have been described in association with colloid cysts, and attributed to temporary occlusion in the ventricular system, although in view of the proximity of the hypothalamic sleep centre it has been suggested that other factors have to be considered.

Weisenburg (1911) published the first series of third ventricle tumours,

and attempted to define a third ventricle clinical syndrome. Since then attempts have been made to amplify his findings in the light of recent publications of new cases. Fulton and Bailey, in summing up this question, believe that ' there is no syndrome of the third ventricle, per se, but tumours immediately affecting this cavity may cause characteristic symptoms by pressure upon its walls and their contained nuclei and tracts. Among the well-recognized syndromes due to lesions of these structures we may mention: (1) the infundibular syndrome (polyuria, adiposity); (2) the syndrome of the central grey matter around the posterior end of the third ventricle and aqueduct of Sylvius (hypersomnia); (3) the thalamic syndrome (central pain, painful hyperæsthesia); (4) the extrapyramidal syndrome (bradykinesia, rigidity); (5) the decerebrate syndrome (hypertonicity, Magnus-de Kleijn reflexes; (6) the syndrome of Parinaud (paralysis of conjugate vertical movements of the eyeballs); (7) the syndrome of the body of Luys (hemichorea; vide Martin, 1927, Ewald, 1891); (8) the hypopituitary syndrome (infantilism, hypotrichosis, lowered metabolism); (9) the uncinate syndrome (olfactory and gustatory symptoms; vide Herzog, 1929), etc.' A number of these syndromes—often incomplete—have been found in a few cases to be associated with colloid cysts. It has been indicated however that, while there are often striking manifestations when the floor and lateral walls of the third ventricle are involved by tumours, there are practically no signs pointing to a lesion of the upper part or the roof of this cavity. Högner (quoted by Fulton and Bailey) states: ' Tumours extending into the third ventricle from the roof are remarkable for their lack of symptoms.' The majority of the colloid cysts in this region—as in the present case—appear to have their origin in the roof of the third ventricle, and this accounts for the absence of localizing signs (excluding ventriculographic findings) in most of the cases.

Pathological.—Colloid cysts of the third ventricle are rare and their ætiology obscure. Most of the argument as to their pathology has centred round the question whether they are of ependymal or of choroid plexus origin. Drennan (1929) describes two cases with local features almost identical with those of our case, and believes them to be of choroid plexus origin, a view that is supported by the finding, in one of his cases, of a second much smaller cyst attached to the choroid plexus of the right lateral ventricle. Byrom and Russell (1932), in describing one case, believed that the cyst was ependymal on the grounds that the lining epithelium showed occasional tufts of cilia. But Zimmerman and German (1933) point out that the finding of cilia in these cysts is not conclusive evidence that they are of ependymal origin, because in the embryo the cells covering the choroid plexus also bear cilia. Certain of these cysts appear to develop above, and to be covered inferiorly by the velum interpositum (Hall, 1913; Fulton and Bailey, 1929; Byrom and Russell, 1932), but such cysts may have developed in the choroid plexus of the lateral ventricle and slipped through the foramen of Munro to

come to lie in the third ventricle as described by Hall. The finding of a cyst with ciliated epithelium in this position led Sjövall (quoted by Fulton and Bailey) to suggest it arose from the paraphysis, which is a rudimentary structure in man projecting into the anterior part of the third ventricle, and this is a view that cannot at present be disputed.

We are content, however, to consider our cyst as originating in the choroid plexus when we take into account the similarity of its epithelium with that of the choroid plexus and the clear association of the connective tissue of the cyst wall with the vascular stroma of the plexus.

The association of a cyst in this position with polycystic disease of the kidneys is of interest as it substantiates the impression, generally existing, that the former condition is ' congenital ' ; that it is, in other words, a local manifestation of an aberrant developmental process whereby certain glandular or epithelial-lined spaces are snared off, with the occurrence, sooner or later, of cystic dilatation. Kauffmann (1929) supports the view that such a process is responsible for the majority of congenital cystic kidneys. He describes it as ' a failure of certain urinary tubules to become patulous, followed by cyst formation.' It is easy to believe in such an origin when one is presented with a microscopical picture like that shown in fig. 3.

Polycystic kidney is quite often only one of many congenital malformations. A case in point recently came within the practice of this laboratory in which a fœtus presented the peculiarities of a polycystic right kidney, micrencephaly, bilateral cleft palate and a bicornuate uterus.

SUMMARY

(1) A case of colloid cyst of the third ventricle is described and the symptomatology discussed.

(2) The pathology of this condition and its relation to cystic disease of the kidney, which was also present, are considered.

(3) It is believed that the majority of these third ventricle cysts are congenital and due to a developmental malformation of the choroid plexus.

We are indebted to Dr. T. B. Davie for assistance in the preparation of this paper, and for allowing us to quote his case of multiple congenital abnormalities.

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Short Notes and Clinical Cases

NARCOLEPSY AND THE MACHINE AGE; THE RECENT INCREASE IN THE INCIDENCE OF NARCOLEPSY

By

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Cases of narcolepsy were exceedingly rare until after the war, since when the frequency of reported cases has increased at an astonishing rate. I know of but 4 cases reported in the past century; in 1901–1910 4 cases were reported; in 1911–1920, 13 cases; and in 1921–1930, approximately 120 cases. Ordinarily one might ascribe this increase to growing familiarity with the syndrome on the part of physicians. When, however, experienced neurologists like Kinnier Wilson [5] and Spiller [4] report that though they have been looking for cases for many years they saw few or none until recently, it is difficult to resist the conclusion that the increase is real and not illusory. Assuming this conclusion to be correct, I propose to consider what might be the explanation for this remarkable increase.

In a previous paper [2] I sought to show that the phenomena of narcolepsy may be interpreted in the light of Pavlov's studies on 'internal inhibition.' It seems permissible to assume that the narcoleptic patient possesses a brain in which inhibition occurs with undue ease, the character of the symptoms depending in part on the extent of the area inhibited. We must therefore ask: Do the conditions of modern life favour the occurrence of inhibition? I shall try to show that they do.

As the first item in the execution of this purpose, I shall call attention to the significance of an observation reported by many narcoleptics, viz., that they fall asleep while driving an automobile. On first thought, one might account for this phenomenon by saying that driving for any distance is monotonous even to a healthy man, and that the narcoleptic, with his abnormal tendency to fall asleep, merely succumbs with undue ease. This explanation, I believe, begs the question, since by definition 'monotonous' applies to those circumstances under which one becomes bored or sleepy. Viewing the matter realistically, one must say that sleep, as shown by Pavlov, represents the irradiation of inhibition of a sufficiently large area of the cortex. One must therefore ask: Does driving favour the spread of inhibition? Let us therefore inquire into the nature of driving, in so far as cortical inhibition is concerned.

The manipulations incident to driving an automobile represent a set of conditioned reflexes. For example, when the driver sees an object in his path, he presses his foot on the brake or steers to one side, or he merely sounds his horn ; it is self-evident that these reactions represent conditioned, rather than unconditioned, reflexes. To say that one man is a better and safer driver than another is to say, in effect, that the one has acquired a more elaborate set of conditioned reflexes than the other.

The seasoned driver has acquired not only many positive conditioned reflexes, but also many negative, or inhibitory, reflexes. As an example, let us consider the reaction of a driver to the sound of an automobile horn. In a person driving an automobile for the first time, the sound of a horn evokes regularly a positive defence reflex ; moreover, other sounds only remotely resembling that of an automobile horn may evoke the same reflex, so that the beginner at the wheel may react with defensive movements even to the sound of a factory whistle. When ' differentiation ' has reached a certain point, the driver now reacts to the horn, but not to the whistle. In the course of time differentiation goes still further, so that now the driver reacts to a horn under some circumstances, but not under others. For example, when the seasoned driver, approaching a cross-roads, hears the sound of a horn apparently coming from the side street which he is nearing, the positive reflex appears (i.e. he slows down and assumes an attitude of greater alertness) ; when, however, on an unintersected highway he hears the same sound coming from the rear, the positive reflex is inhibited (i.e. he makes no defensive movements, his only response, if any, being to drive to one side to permit the driver in the rear to pass). This is a perfect analogue to the situations confronting Pavlov's dogs in his experiments on differentiation. Such situations occur many times an hour during ordinary conditions of driving. Indeed, to picture a driver in whose cortex the occurrence of differentiation is reduced to a minimum, one would have to picture him on a wide and perfectly straight unintersected highway where by prearrangement and with his knowledge there are no obstacles, no traffic, and no pedestrians. Here the driver would have relatively little need of being alert. But under ordinary conditions the cortex of the driver is continually called upon to differentiate a multitude of ' compound stimuli,' some of which call forth positive, others negative, conditioned reflexes.

These considerations, I believe, warrant the statement that when sleep occurs during driving, it is not because of monotony, but because the differentiation constantly going on in the cortex gives rise to an ever-increasing tide of inhibition which finally overwhelms the substrate of consciousness. The man who falls asleep at the wheel is strictly comparable to the dog which falls asleep during an experiment on differentiation.

In my paper [3] on some military aspects of narcolepsy, I referred to the fact that during the war soldiers sometimes fell asleep on sentry duty. The sentry and the automobile driver are each in situations calling for the

differentiation of stimuli, and they fall asleep from identical physiological causes.

Since driving seems to favour the occurrence of inhibition, one might ask whether there are cases in which there seems to be a relationship between excessive driving and the onset of narcolepsy. It is to be hoped that physicians who have narcoleptic patients under their care will inquire into this point. At present I know of only one case in which such a relationship seems to have existed—Case II reported by Harding and Berg.[1] The patient, a business man, attributed the onset of his narcoleptic symptoms to 'auto-intoxication due to the fact that I'd driven about 600,000 miles in the four or five years previous.' Since the figure seemed excessive, I wrote to Dr. Harding, who informed me that it is a misprint; it should be 100,000. Even 100,000 miles in four or five years represents a lot of driving, and many healthy people would find it taxing in the extreme; for a potential narcoleptic, with his greater tendency to cortical inhibition, it might well have proved to be the final straw that caused the symptoms to make their first appearance. I therefore consider it possible that the patient of Harding and Berg was not wrong when he designated his many miles of driving as a precipitating factor.

So far my remarks have been confined to drivers. Corresponding statements may also be made of pedestrians. Crossing the road in the era of horse-drawn vehicles required no very great degree of alertness; crossing the street today is a venture fraught with peril. The pedestrian, like the driver, at frequent intervals differentiates stimuli. Thus, when he is on the street, the sound of a horn evokes a positive defence reflex; when he is on the sidewalk, the same sound is followed by inhibition of the same reflex. Here is differentiation of compound stimuli. To take another example: if, while crossing the street, the pedestrian sees an automobile 50 yards away moving toward him at an apparent speed of 40 miles per hour, the positive defence reflex appears; if at the same distance he sees an automobile coming toward him at a speed of only 10 miles per hour, the positive reflex is inhibited, the pedestrian knowing that he does not need to hurry. This situation is comparable to that of the laboratory animal in which there is differentiation of tuningforks of different wavelengths.

The statements made about the driver and the pedestrian may be generalized to apply to *all people who work with, or in the vicinity of, life-threatening machinery.* When a working-man learns to obey a set of directions in order to avoid being mangled by his machine, he in effect acquires a set of positive and negative conditioned reflexes.

Thus one reaches the conclusion that people living in a modern civilized community must acquire conditioned defence reflexes to a far greater extent than their grandfathers. Our grandfathers were comparatively rarely in situations requiring instant and precise adjustment to dangerous mechanical forces; today such situations confront the majority of us many times a day.

This means a corresponding increase in the amount of cortical inhibition to which we are subject. Obviously, in 50 years the human cortex has not evolved to a degree comparable with the increased burden imposed on it by the 'Machine Age.' Nevertheless (so liberal is Nature in providing us with margins of safety), in the vast majority of people this increase in inhibition is compensated for; these people are clinically well.* Of the remaining minority, some are so constituted that they would have developed symptoms of narcolepsy even under the simplest conditions of life. But there must be others in whom the morbid tendency is not so pronounced, with the result that today they have symptoms which would have remained latent had they lived 50 years ago. I suggest that this would explain the tremendous increase, in recent years, in the incidence of narcolepsy.

It should be emphasized that, so far as cortical inhibition is concerned, the significant thing about present-day life is the prevalence of conditioned *defence* reflexes, and not just of conditioned reflexes in general. Conditioned reflexes existed long before the age of machinery. Any learning process means, physiologically, the acquisition of a set of conditioned reflexes. Thus, when a child learns to eat peas with a fork and not a spoon, he has acquired two conditioned reflexes, one positive and one negative. But these reflexes, which do not pertain to the physical preservation of the individual, are, from the point of view of the ætiology of narcolepsy, of infinitesimal significance in comparison with the defence reflexes discussed in this paper. The excitations correlative with the act of eating peas with a fork are weak in comparison with the excitations which enable a pedestrian to jump clear of the automobile that is upon him. Correspondingly, the inhibitions correlative with the avoidance of the spoon are weak in comparison with the inhibitions by means of which the pedestrian checks his walking movements when these movements, uninhibited, would bring him directly into the path of a moving vehicle close by. The argument of this paper, therefore, may not be attacked on the ground that we have always had conditioned reflexes. Conditioned reflexes we have always had, but conditioned defence reflexes, with their powerful excitations and equally powerful inhibitions, we never had in such profusion prior to the present era of the machine.

SUMMARY

The widespread use of life-threatening machinery has resulted in a vast increase in the number of conditioned defence reflexes acquired by the

* I have reference here only to the more severe clinical manifestations of inhibition, such as sleep attacks and cataplexy. If we knew more about the milder clinical manifestations of inhibition, we might find them very widespread indeed. For example, there is some reason to believe that fatigue may occur as a manifestation of inhibition,[3] in which case we might well suspect that while the 'Machine Age' is causing only a few hundred people to develop the major symptoms of narcolepsy; it is causing many millions to suffer from increased fatigue.

majority of civilized mankind. The frequent occurrence of these reflexes and, especially, the frequent occurrence of differentiation must result in an increase in the amount of cortical inhibition occurring in most people. The case of the automobile driver is chosen as an example to demonstrate concretely the validity of these statements. It is to these circumstances that one may plausibly attribute the vast increase in the incidence of narcolepsy in the past two decades.

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SUPPLEMENTARY NOTE

After this article was accepted by the Editor of the JOURNAL, I came across a recent article by M. S. Kaplinski ('Anfälle von kurzweiligem Einschlafen bei Transportführern,' *Zeits. f. d. g. Neurol. u. Psychiat.*, 1933, **147**, 101). Kaplinski calls attention to the frequency with which sleep attacks occur in chauffeurs and street-car motormen. This frequency is so great that the authorities of the Moscow street railways have asked the Institute for Industrial Hygiene to make a study of the matter—a fact of great interest in view of the discussion offered in my paper.

On one point I must disagree with Kaplinski. In explaining the sleep attacks occurring in drivers of vehicles, he alludes to the fact that passengers frequently fall asleep, seemingly through the influence of the monotonous sounds and rockings of a moving conveyance. He clearly implies (in several places) that the somnolence of the driver is brought on by the same monotony which lulls the passenger to sleep. But, instead of being comparable, the situations of the passenger and the driver differ tremendously in their physiological import. The passenger relaxes; he makes no effort to 'take in' stimuli. The driver, on the other hand, 'strains his attention' to the utmost; he strives to see and hear everything, and, as I have already tried to show, there is in his case continual differentiation of positive and negative stimuli. I am not prepared to formulate the causes of the somnolence that overtakes the passenger, but, whatever they are, I should for the present regard them as negligible in their bearing on the somnolence of the driver.

Editorial

CHANGING CONCEPTIONS OF EPILEPSY

PRESENT-DAY research in respect of epilepsy is concerning itself principally with the experimental induction of fits, with discovery of the physicochemical changes accompanying them, and with their control by other methods than the purely medicinal. The result is that timeworn theories are undergoing revision, but less attention is being devoted to underlying questions as to the meaning of the term, the limitations of the disorder, and the inclusion or exclusion of certain types of clinical phenomena.

The traditional view is based on the contention that a disease called epilepsy exists, its salient symptom being the occasional fit. This disease is alleged to be progressive, rather intractable, and prone to result in mental deterioration. Its cause being unknown, it is labelled ' idiopathic,' in contrast with well-recognized morbid states often disclosed by similar fits, e.g. cerebral vascular disease, brain tumour, encephalitis, and so forth. But we may think it curious that the patently symptomatic nature of many types of fit has not yet sufficed to rouse suspicion as to the ' idiopathic ' variety—at least, not universally ; the untenable character of the ' idiopathic ' hypothesis has convinced some but not all observers. Those who do not like the term sometimes use the expression ' genuine ' or ' essential ' to characterize the ' disease,' as though fits of a symptomatic kind were merely casual or in some unexplained way ' false.' The best present-day opinion is none the less veering round in the direction of affirming that all epilepsies are symptomatic, inclusive of that variety whose basis still eludes search, and that since some causes are known the cause of the latter will eventually be revealed in its turn. Instead of the term ' epilepsies ' it might be preferable to employ alternatives of more non-committal nature, e.g. ' paroxysmal disorders ' or ' convulsive states '—a series of diverse conditions linked together by the occasional occurrence of ' fits,' but at the risk of perpetuating notions inherited from a less well-informed era the word will doubtless continue in vogue. For didactic purposes, too, it may be temporarily expedient to differentiate

epilepsy ' of unknown origin ' in some terminological way, however undesirable from the standpoint of pathogenesis and physiology.

If nosological and connotative difficulties are provisionally settled by considering all varieties as symptoms or syndromes only, and none as a ' disease,' we are faced by the cognate problem of defining what constitutes a fit. It is open to the clinician to claim any transient, paroxysmal, disorderly, uncontrolled, and recurrent manifestation of any neural process as in essence a ' fit,' and this on any physiological plane. In its ordinary acceptation the word stands for conditions as far apart as convulsive twitches in a limb segment and highly co-ordinate acts of the whole person, sometimes of no little duration, comprised under the term of ' hysterical fits.' These are by no means always paroxysmal or disorderly. Again, while all fits are uncontrolled, some are not specially short, e.g. partial continual epilepsy ; hence not all epileptic discharges are brief, though brevity is held to constitute a cardinal feature of the state. Once more, it is permissible to regard absence of movement as a feature of some fits ; therefore not all epilepsies are convulsive. A ' convulsive fit ' is not a redundant phrase. As is well known, too, the ' man in the street ' talks of a ' fit of the blues,' a ' fit of temper,' of ' sneezing,' of ' laughter '—occurrences which seem poles apart from ordinary ideas of ' epileptic ' fits, and yet which share in some at least of the characters specified above. In regard to the major epileptic fit itself its features are more or less stereotyped, no doubt ; they comprise rapidity of onset, absence of control, interruption of the stream of consciousness, crudity, transience, reversibility, etc. ; yet some of its component parts do not comply with the scheme. The aura often enough is neither ill-regulated nor excessive in intensity or other quality ; it may consist of a crudity such as a sudden overpowering stench, but on the other hand, it may equally well consist of an elaborate visual scene or memory which is admittedly ' pleasant.' Moreover, some movements of certain attacks are quasipurposive and co-ordinate, devoid of all convulsive element ; those of petit mal, which is ' pure ' epilepsy, are neither violent nor exaggerated. As for fits implicating visceral centres, there may be no interference with consciousness, no involvement of skeletal muscles, and, in fact, none of the customary signs of ' epilepsy,' so that divergence from the formula may be extreme. Yet not only do such visceral attacks occur, but accompaniments of an identical kind are accepted without cavil in any major case, e.g. hyper-

idrosis, cyanosis, sialorrhœa, pallor, and so on. It appears neither inconceivable nor absurd that some bouts of tachycardia, diarrhœa, polyuria, etc., even of neuralgia, might be registered in the class.

Contemplation of the epileptic field can thus scarcely fail to discount in some degree the value of conventional features forming its landmarks. Of these, possibly the least mutable comprise suddenness of onset, brevity of duration, and habit of recurrence. They may be customary in the average case, but, as pointed out above, some varieties are protracted, while repetitions may be extraordinarily infrequent, and even initial abruptness loses significance when the aura is long drawn out, as in some uncinate examples. And what of the epileptic 'borderland,' with its migraines, vertigos, narcolepsies, cataplexies, and the rest? Their clinical expression includes features of similar or identical kinds; hence to erect standards even in regard to the main types of epileptic fit becomes a thankless task. For the present it is wise to eschew schematic definition and allow latitude in respect of epileptic symptoms; however general the agreement on the habitual manifestations of epilepsy, any endeavour to circumscribe it by a series of Procrustean slices transgresses current views on the nature of disease.

Abstracts

Neurology

NEUROANATOMY AND NEUROPHYSIOLOGY.

[1] **On the nature of inhibition : a review.**—W. R. Ashby. *Jour. of Ment. Sci.*, 1934, **80**, 198.

Many theories of inhibition are here collected and reviewed, but the majority have to be rejected at once in the light of present-day knowledge. From the examination of the data the 'humoral' theory is regarded as far above the others. This theory has previously been discussed in relation to the spinal reflexes but is discussed here in view of its wider implications. It is shown that this theory offers a satisfactory explanation of some difficulties in the concept of 'physiological levels' and gives a solution of the problem of 'back-control' between levels. The law of forward direction is found to follow at once from this theory, and various microscopical morphological appearances are shown to be just the type of mechanism required by it. Also Pavlov's 'irradiation' and 'concentration' are thus easily explained. Integration in behaviour is compared with the same process in growth, and it is suggested that the ultimate mechanisms are probably identical. Some of the factors known to be of importance in growth are considered, and it is shown that the 'humoral' theory provides the counterpart in behaviour. The clinical applications are discussed.

C. S. R.

[2] **Labyrinth and cortex.**—E. A. Spiegel. *Arch. Neurol. and Psychiat.*, 1934, **31**, 469.

With a view to determining whether labyrinthine impulses enter the cortex, the author studied the changes of electrical potentials in the cortex by stimulation of the labyrinth.

Rotation increased the currents, which were led off from the dorsal part of the posterior suprasylvian and ectosylvian gyri in cats under curare paralysis or bulbocapnine catalepsy. Such an effect was not prevented if the eyes were closed, the vagi or the uppermost segments of the spinal cord severed, or the frontal lobe with the motor zone or the parietal lobe extirpated. In deep ether anæsthesia, after bilateral labyrinthectomy or after an incision into the white matter severing the connection of the posterior suprasylvian and ectosylvian gyri with the subcortex, the electrogram of these

gyri was not changed by rotation. A postrotatory increase of the potentials in the parietal lobe depends on the intactness of the posterior suprasylvian and ectosylvian gyri and of the frontal lobe; after combined extirpation of the frontal and the temporal lobe, rotation could no longer increase the currents led off from the parietal lobe. Postrotatory electrical disturbances were noticed in the frontal lobe even after extirpation of the temporal lobes, but a definite effect of the rotation was no longer observed if this extirpation was combined with high transverse section of the spinal cord. The experiments seem to indicate that labyrinthine impulses can enter the cortex, particularly parts of the temporal lobe near the parietal lobe. It is also possible that rubrothalamofrontal tracts are used as a common path by the labyrinthine as well as by other impulses.

R. M. S.

[3] **Hypothalamus and temperature control.**—H. C. Bazett, B. J. Alpers and W. H. Erb. *Arch. Neurol. and Psychiat.*, 1933, **30**, 728.

The histological evidence here advanced supports the hypothesis of the importance of the hypothalamic area in temperature control. Animals whose brainstems had been subjected to anterior decerebration had the capacity of reacting to cold and of regulating their own body temperature at a normal level (and probably of developing fever) in the absence of the corpus striatum and thalamus, which were not therefore essential. The presence or absence of temperature control appeared to be associated with the preservation of the hypothalamus just cephalic to the corpora mamillaria; the area included the nuclei surrounding the walls of the third ventricle and the infundibular nuclei. Such animals did not, however, show a normal hyperpnœa when exposed to excessive heat.

R. M. S.

[4] **The diencephalon-hypophysis system** (Zur Frage des Zwischenhirn-Hypophysensystems).—O. Gagel und W. Mahoney. *Zeitschr. f. d. g. Neurol. u. Psychiat.*, 1933, **148**, 272.

The anatomical researches of Greving and Pines favour a connection between the posterior lobe of the hypophysis and the nucleus supraopticus.

The authors have extirpated the hypophysis in animals and have subsequently carried out microscopical examinations for retrograde cell alterations in the nucleus supraopticus and in the nucleus paraventricularis. Alterations in the cells of these nuclei could not be detected, consequently experimental research concerning this question is not in favour of the results of normal anatomy.

M.

NEUROPATHOLOGY

[5] **Acromegaly and von Recklinghausen's disease** (Acromegalie et maladie de Recklinghausen).—A. DE CASTRO. *Rev. neurol.*, 1934, **41**, 39.

DE CASTRO comments on the association of acromegaly with von Recklinghausen's neurofibromatosis and refers to some 12 cases recorded in the literature, including one which he described in 1916. It is pointed out that modern radiological investigations have advanced our knowledge of the bony disorders of this malady. The bony changes may be placed in two distinct groups :

1. Disorders of development of no characteristic type, such as defects of ribs, vertebral anomalies and the formation of exostoses.

2. Bony changes characteristic of neurofibromatosis which depend directly or indirectly upon the disease, e.g., atrophy and hypertrophy, local erosion from pressure exerted by neurofibromata, and osteoporosis of the vertebræ. In the cases associated with acromegaly there was evidence of an intrasellar tumour as shown either by radiological examination or at autopsy. This association is not considered to be merely one of two distinct morbid conditions occurring by chance in the same individual but a definite pathological association between two diseases.

C. W. D.

[6] **The changes in the concentration of inorganic calcium and phosphorus during convulsions of experimental origin, in cats, before and after thyroparathyroidectomy, with and without bromide therapy.**—HELEN C. COOMBS, DONALD S. SEARLE and F. H. PIKE. *Amer. Jour. Psychiat.*, 1934, **13**, 761.

THE minimal convulsant and total dosage of a drug needed to elicit convulsions is much less in cats after thyroparathyroidectomy than in control animals. The number of electrical excitations of the cortical motor area possible in cats after thyroparathyroidectomy is much smaller than in controls. The number of occlusions of the head arteries which can be done in animals after thyroparathyroidectomy is also much smaller than in controls. The administration of sodium bromide for two weeks before thyroparathyroidectomy prevents postoperative tetany, and, if continued, prolongs life for at least three or four weeks without other remedial measures. In cats after thyroparathyroidectomy, the calcium-phosphorus ratio is almost 50 per cent. lower than in controls. This ratio in cats under bromides before operation is, however, less changed and may even approach the ratio of the controls. While there is always a rise in calcium and phosphorus of the blood serum following experimentally induced convulsions, both in controls and after simple thyroparathyroidectomy, previous administration of bromides causes a fall of calcium and phosphorus following convulsions, in both sets of conditions.

C. S. R.

SENSORIMOTOR NEUROLOGY

[7] **General localization of epileptic manifestations.**—Wilder Penfield and Lyle Gage. *Arch. Neurol. and Psychiat.*, 1933, **30**, 709.

In this study the authors have analyzed 75 cases of focal epilepsy in which careful study revealed no local sign. In nearly all cases cerebral pneumography was carried out and the patient was operated on under local anæsthesia. The seizures studied were either spontaneous or induced by hyperpnœa, by hydration or by direct cortical stimulation.

The principal conclusions may be summarized as follows :—

The most frequent lateralizing sign is deviation of the head and eyes to the side opposite the hemisphere involved. Seizures which have their origin in the frontal lobe are usually characterized by loss of consciousness (without aura) and turning of the eyes, head and body to the opposite side, followed by nearly simultaneous convulsion of the opposite extremities, falling and generalization of the attack. In seizures which arise in the precentral or postcentral gyrus consciousness is usually lost late. A ' tingling sensation ' may follow a Jacksonian ' march,' just as movement follows in seizures arising in the frontal lobe. Consciousness is likewise apt to be lost late in seizures arising anywhere behind the central sulcus, and such seizures are, of course, ushered in by auras. It must be remembered, however, that a major attack may leave retrograde amnesia, so that the aura is forgotten. In such circumstances the aura may be remembered only in slight seizures which do not progress to generalization.

Certain ' epileptiform patterns ' have often been described, such as so called temporosphenoidal fits and attacks arising in the occipital lobe beginning with lights or darkness in the opposite visual field. But the authors have pointed out that seizures originating in the supramarginal gyrus in area 7a, possibly extending to areas 19 and 22, are characterized by a discontinuous twinkling of lights seen in the contralateral field without any involvement of the calcarine zone.

An aura of pain or of epigastric distress may arise from activity of the cerebral cortex, and cortical stimulation reproduces such sensory phenomena. The buzzing sounds and the dizziness which are characteristic of unilateral temporal lobe seizures have been reproduced by electrical stimulation, but the more complicated dream states and odours have never been reproduced, perhaps because of the limitation of surgical approach.

It should be noted further that involvement of a large artery, such as occurs when a glioma surrounds the origin of the artery, may give rise to an epileptiform seizure beginning at a distance from the primary lesion but within the distribution of the artery.

Finally, cerebral localization of epileptic manifestations is necessary for the interpretation of convulsive seizures and is of obvious importance in cases in which radical therapeutic measures are indicated.

R. M. S.

[8] **The influence of emotion in precipitating convulsions.**—Frank Fremont-Smith. *Amer. Jour. Psychiat.*, 1934, **13**, 717.

Forty-two unselected patients with ages varying from 10 to 53 years were studied to determine how frequently emotion acts as a precipitating factor. All suffered from generalized convulsions with loss of consciousness. In 31 a direct relationship was found. In several instances all or nearly all the attacks have been immediately preceded by strong emotion, usually fear, guilt or frustration. In eight, major or minor attacks were precipitated under observation by a discussion of the emotional difficulty. In three, attacks could apparently be precipitated by the physician at will by such discussion. In some cases the relation of the disturbing emotion to the attack was obvious and clearly evident to the patient. More often he was unaware of the relationship, particularly when there was a strong tendency to suppress the emotion from consciousness. In many psychotherapy was of definite value and insight gained of the relationship of the emotion to the attack was followed by a marked reduction in the number of convulsions as well as a decided change in the patient's outlook on life. Many of these had definite evidence of organic brain disease. The theory that stimulation of the sympathetic nervous system by emotion plays an important rôle is supported by the fact that convulsions were occasionally precipitated by pain and by cold. Moreover, the onset of acute infections frequently precipitates attacks in predisposed individuals. Here again the sympathetic is strongly stimulated. Whether such stimulation does this by cerebral vasoconstriction or by some other mechanism is not known.

C. S. R.

[9] **The narcolepsies.**—J. Notkin and S. E. Jelliffe. *Arch. Neurol. and Psychiat.*, 1934, **31**, 615.

The authors emphasize that narcolepsy is not a disease per se, but a group of symptoms that may occur under a variety of conditions. They classify the cases reported in the literature into the following five groups: (1) Attacks of sleep and hypersomnia in psychoneuroses, in manic-depressive psychoses and in schizophrenia; (2) narcoleptic attacks in chronic epidemic encephalitis; (3) narcoleptic attacks in cases of involvement of the central nervous system, exclusive of group 2, and in cases of somatic disease; (4) attacks in combination with convulsive (epileptic) attacks; (5) attacks in cases in which there are no definite signs pointing to organic pathological changes. The cases in group 5 are designated as the cryptogenic type of narcolepsy.

Seven personal observations of the symptomatic and cryptogenic types are described. The symptom-complex is discussed. It is believed that only in the cryptogenic group are both types of attacks, the narcoleptic and the cataplectic, present, while in the symptomatic variety one or the other type

of seizures is prevalent. A review of the current theories of the process of sleep is made.

The ætiological and pathogenic possibilities are discussed, and it is suggested that the narcolepsies are closely related to the epilepsies. This supposition is made on the basis of the following considerations: (1) The paroxysmal nature of the narcoleptic attacks; (2) the occasional occurrence of various types of aura preceding the attack; (3) the hyperkinetic manifestations reported during the narcoleptic attacks; (4) the confusional states reported at times as following the attacks; (5) the mixture of both types of attacks—the narcoleptic and the epileptic—in the same person; (6) the occasional transition of narcoleptic manifestations into epileptic seizures and vice versâ; (7) the epileptic heredity in some instances; (8) the fact that similarly to the epilepsies there are the symptomatic and the cryptogenic types of narcolepsies.

R. M. S.

[10] **Narcolepsy.**—Luman E. Daniels. *Medicine*, 1934, **12**, 1.

Here we have a wide review of the subject in over a hundred pages. In a study of 377 cases of narcolepsy, the findings of other observers relative to the frequency of onset in adolescence and early adult life were confirmed. In a larger group of 439 cases, males outnumbered females by roughly 2 : 1. Numerous ætiological factors, including heredity, preceding infection and injuries to the head are considered. All postinfectious cases were not necessarily assumed to be encephalitic. Symptomatic narcolepsy may differ in no way from the idiopathic form. The possible existence of constitutional factors in cases belonging to both groups could not be denied. It finally became apparent that the essential anatomical or functional changes might owe their origin to a variety of factors. The main manifestations of the disorder appear to be interrelated, and the hypothesis that all represented states of partial inhibition, similar if not identical with sleep, seemed supported by clinical observation. Disturbances of nocturnal sleep warranted the conclusion that the sleep-regulating function may be profoundly affected. Gaining weight was common in its course, and sexual disturbances, though infrequent, were considered of some significance. Changes of personality were not often noted. Although not inconsistent with a long and healthy life, the malady took a chronic course; considerable betterment in the severity of the symptoms was not common.

The various methods of treatment are reviewed, the symptomatic relief afforded by the administration of ephedrine sulphate being considered in some detail. The assumption, based entirely on reasoning by analogy, that the malady is attributable to a disturbance in the floor of the third ventricle seems most likely.

C. S. R.

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C. S. R.

[9] **The narcolepsies.**—J. Notkin and S. E. Jelliffe. *Arch. Neurol. and Psychiat.*, 1934, **31**, 615.

The authors emphasize that narcolepsy is not a disease per se, but a group of symptoms that may occur under a variety of conditions. They classify the cases reported in the literature into the following five groups: (1) Attacks of sleep and hypersomnia in psychoneuroses, in manic-depressive psychoses and in schizophrenia; (2) narcoleptic attacks in chronic epidemic encephalitis; (3) narcoleptic attacks in cases of involvement of the central nervous system, exclusive of group 2, and in cases of somatic disease; (4) attacks in combination with convulsive (epileptic) attacks; (5) attacks in cases in which there are no definite signs pointing to organic pathological changes. The cases in group 5 are designated as the cryptogenic type of narcolepsy.

Seven personal observations of the symptomatic and cryptogenic types are described. The symptom-complex is discussed. It is believed that only in the cryptogenic group are both types of attacks, the narcoleptic and the cataplectic, present, while in the symptomatic variety one or the other type

of seizures is prevalent. A review of the current theories of the process of sleep is made.

The ætiological and pathogenic possibilities are discussed, and it is suggested that the narcolepsies are closely related to the epilepsies. This supposition is made on the basis of the following considerations: (1) The paroxysmal nature of the narcoleptic attacks; (2) the occasional occurrence of various types of aura preceding the attack; (3) the hyperkinetic manifestations reported during the narcoleptic attacks; (4) the confusional states reported at times as following the attacks; (5) the mixture of both types of attacks—the narcoleptic and the epileptic—in the same person; (6) the occasional transition of narcoleptic manifestations into epileptic seizures and vice versâ; (7) the epileptic heredity in some instances; (8) the fact that similarly to the epilepsies there are the symptomatic and the cryptogenic types of narcolepsies.

R. M. S.

[10] **Narcolepsy.**—Luman E. Daniels. *Medicine*, 1934, **12**, 1.

Here we have a wide review of the subject in over a hundred pages. In a study of 377 cases of narcolepsy, the findings of other observers relative to the frequency of onset in adolescence and early adult life were confirmed. In a larger group of 439 cases, males outnumbered females by roughly 2 : 1. Numerous ætiological factors, including heredity, preceding infection and injuries to the head are considered. All postinfectious cases were not necessarily assumed to be encephalitic. Symptomatic narcolepsy may differ in no way from the idiopathic form. The possible existence of constitutional factors in cases belonging to both groups could not be denied. It finally became apparent that the essential anatomical or functional changes might owe their origin to a variety of factors. The main manifestations of the disorder appear to be interrelated, and the hypothesis that all represented states of partial inhibition, similar if not identical with sleep, seemed supported by clinical observation. Disturbances of nocturnal sleep warranted the conclusion that the sleep-regulating function may be profoundly affected. Gaining weight was common in its course, and sexual disturbances, though infrequent, were considered of some significance. Changes of personality were not often noted. Although not inconsistent with a long and healthy life, the malady took a chronic course; considerable betterment in the severity of the symptoms was not common.

The various methods of treatment are reviewed, the symptomatic relief afforded by the administration of ephedrine sulphate being considered in some detail. The assumption, based entirely on reasoning by analogy, that the malady is attributable to a disturbance in the floor of the third ventricle seems most likely.

C. S. R.

XUM

[11] **Cerebral localization in cerebrovascular disease.**—CHARLES DAVISON, S. PHILIP GOODHART and WILLIAM NEEDLES. *Arch. Neurol. and Psychiat.*, 1933, **30,** 749.

THIS paper is limited to a simple exposition of disturbances of function in cases of cerebral vascular disease and alterations in the brain in these cases, with a view to establishing a parallelism in the findings. The authors have not discussed the various doctrines regarding localization of function in the brain, or weighed the validity of the beliefs of strict localizationists (Broca, Wernicke and others) as against those, who, though accepting the presence of specific functional areas established by neurophysiology and other methods, argue for a more diffuse representation for cerebral functions (H. Jackson, von Monakow, K. Goldstein, S. Freud and H. Head). The objective anatomical approach, even at this late date and after the accumulation of so many observations, is still a necessary method of procedure. That two such authorities as Henschen and Niessl von Mayendorf, after studying about 1,200 cases of motor aphasia, clinically and pathologically, concluded by localizing the function in two different regions is ample evidence of the truth of this statement. Anatomy must still provide the moorings for soaring psychological speculations. On the other hand, the organicist must not remain unmindful of the dictum of Hughlings Jackson, who insisted that because a lesion in a certain area creates disturbances of a certain function it does not follow that the function is localized in that area.

As was stated at the outset, cerebral localization on the basis of vascular supply, though difficult and necessitating caution in interpretation, can still be definitely established. The authors were able, on the basis of a study of 48 cases, to demonstrate definite syndromes accompanying occlusion of the anterior and middle cerebral arteries or their branches; in cases of partial occlusion of the posterior cerebral artery the resultant quadrantic visual field defect was pointed out.

R. M. S.

[12] **Megalencephaly with diffuse glioblastomatosis of the brainstem and the cerebellum.**—ARTHUR WEIL. *Arch. Neurol. and Psychiat.*, 1933, **30,** 795.

WEIL reports a case of megalencephaly in a boy, age seven years, whose mental development had been normal up to the sixth year. The brain, which weighed 1,856 gm., resembled that of the case of Marburg reported in 1906, there being a combination of interstitial hyperplasia with diffuse glioblastomatosis and interstitial hypertrophy, demonstrating the intimate relationship between these different processes.

A congenital familial maldevelopment is suggested by the megalencephaly of the still living brother and by the congenital underdevelopment of the

precentral area, the skeletal musculature, and the absence of chromaffin tissue of the medulla of the suprarenal glands.

R. M. S.

[13] **Clinical observations on a case of amaurotic idiocy of infantile type with atypical ocular lesions** (Remarques cliniques sur un cas d'idiotie amaurotique du type infantile avec lésions oculaires atypiques).—C. COHEN and L. VAN BOGAERT. *Jour. de neurol. et de psychiat.*, 1933, **33,** 456.

A CHILD, age 13, showed mental retardation with blindness together with signs of a partial decerebrate syndrome—tonic reflexes of neck and myo-acoustic reflex. He also exhibited epileptic attacks of apparent subcortical origin. Such a syndrome in a child of the Jewish stock gives a diagnosis of amaurotic idiocy. The fundus changes were confined to the peripapillar region; there was no actual lesion of the macula. The authors point out that the ocular changes in juvenile and retarded types of the disease, unlike those of the infantile form, are often atypical.

C. W. D.

[14] **On senile progressive paralysis** (Sulla paralisi progressiva senile).—U. DE GIACOMO. *Riv. di pat. nerv. e ment.*, 1932, **40,** 308.

A CASE is described in which there were combined typical symptoms of the parasyphilitic condition with a senile dementia of mixed type (parenchymatous and arteriosclerotic). This combination illustrates the widespread morphological changes which may be met with in this condition and refutes the assertions that a parasyphilitic change 'prevents the development of certain signs of senile dementia, such as the plaques of Redlich-Fischer and the fibrillary alterations of Alzheimer. The author contributes also some physiopathological and therapeutic suggestions.

R. G. G.

[15] **On a case of chronic non-hereditary chorea** (Su un caso di corea cronica non ereditaria).—T. PREDAROLI. *Riv. di pat. nerv. e ment.*, 1933, **41,** 586.

THE author describes completely both the clinical and pathological features of a case of non-hereditary chronic chorea. In this there appeared demonstrable inflammatory and degenerative lesions, which were apparently progressive, giving the picture of a chronic diffuse myeloencephalitis. It would appear that the spread of the unknown pathogenic agent was by the blood-stream and in all probability also by the cerebrospinal fluid.

R. G. G.

XUM

[16] **Traumatic cerebrospinal fluid fistula** (Die traumatische Liquorfistel)—Müller. *Münch. med. Woch.*, 1934, **81**, 280.

Following a severe trauma of the frontal bone, a young man complained of diminution in visual and olfactory acuity. When he stooped forward clear cerebrospinal fluid escaped from the right nostril. On his remaining in bed for two weeks with the head kept lower than the trunk, the flow of cerebrospinal fluid ceased and the patient felt quite well. Three months later he died suddenly after only one day's illness with symptoms of meningitis. On post-mortem examination an abscess in the frontal lobe of the brain was found. As a rule traumatic cerebrospinal fistulæ arise some days or weeks after the trauma ; seldom as in the above case do they occur immediately after the injury. The risk of infection of the cerebrospinal fluid always has to be considered ; consequently in every case the prognosis is uncertain.

M.

[17] **Postdiphtheritic cerebellar syndrome of a transitory nature** (Un cas de syndrome cerebelleux transitoire postdiphthérique).—F. Meerssemer. *Bull. et mém. soc. méd. hôp. Paris*, 1933, **49**, 379.

Following an unrecognized diphtheritic infection a young adult developed a palatal palsy followed by polyneuritis of all four limbs and a cerebellar syndrome. The condition was accompanied by a mild meningeal reaction, the cerebrospinal fluid showing few cells but increased protein and a colloidal benzoin reaction of meningitic type. The patient made a good recovery.

C. W. D.

[18] **Pseudoneuromyelitis optica, in reality Lichtheim's syndrome** (Fausse neuroptico-myélite, en réalité syndrôme de Lichtheim).—Moriez. *Rev. neurol.*, 1934, **41**, 129.

During the course of a parasitic anæmia and at the time of very difficult labour, a febrile neurological syndrome developed. The symptoms consisted in a sudden amaurosis with double optic neuritis and a flaccid paraplegia with root pains. Subsequently the patient recovered from anæmia and the spinal cord signs disappeared almost completely. The optic neuritis persisted for longer but improved on anti-anæmia treatment.

In spite of the presence of pyrexia the author classifies this case among the 'neuro-anæmic' syndromes. Pyrexia is of little value as a differential symptom between true neuromyelitis optica (infective) and neuro-anæmias with optic and myelitic signs.

C. W. D.

[19] **Clinical and anatomical study of progressive spinal amyotrophy** (Zur Klinik und Pathologie der progressiven spinalen Amyotrophien).—STEFAN. *Jahrb. f. Psychiat. u. Neurol.*, 1933, **49**, 5.

A CASE is described in considerable detail of what appeared to be an example from the clinical standpoint of exclusive chronic anterior poliomyelitis. The subsequent pathological study, however, showed it to be an undoubted case of amyotrophic lateral sclerosis. This observation further confirms the doubt as to the existence of exclusive involvement of the anterior cornual cells in spinal amyotrophies and indicates that the correct view is to include all such cases under the heading of ' motor neurone degeneration.'

C. W. D.

[20] **Syringomyelia or tumour of the spinal cord** (Syringomyelie oder Tumor Medullæ).—L. VAN DER HORST and I. A. VAN HASSELT. *Deut. Zeits. f. Nervenheilk.*, 1934, **133**, 129.

A MAN, age 26 years, somewhat feebleminded, developed a dissociated disturbance of sensibility in the upper limbs. Later, sensation in the lower limbs also became affected and paralysis of both arms and legs gradually supervened. At autopsy it was seen that the entire spinal cord was surrounded by tumour formation and, in addition, at the level of the eighth cervical segment, a small tumour was found within the spinal cord substance. It is probable that the intramedullary tumour was the initial lesion and that later with further growth it penetrated the pial membrane and reached the outside of the spinal cord. There it had gradually spread in the spinal canal and compressed the entire spinal cord. While, at first, the palsy of the lower limbs was a spastic one, in the later stages the paralysis was flaccid with wasting and fibrillary tremors. By cisternal injection of lipiodol it had been ascertained that the upper border of the tumour was in the superior cervical region. Lumbar puncture had yielded no fluid. Had it been possible to examine the cerebrospinal fluid, the nature of the process would probably have been demonstrated. It could not be definitely ascertained by histological examination whether the tumour was a small-celled sarcoma or a medulloblastoma.

M.

[21] **Herpes zoster and herpetic disorders in the region of the ear** (Ueber Herpes Zoster und herpetische Erkrankungen im Ohrgebiet).—L. HAYMANN. *Münch. med. Woch.*, 1934, **81**, 137.

THE following herpetic affections of the aural region may be distinguished:

1. Herpes zoster oticus, in which neither the facial nerve nor the acoustic nerve is affected.

2. Herpes zoster oticus with facial paralysis.

XUM

3. Herpes zoster oticus with involvement of both facial and acoustic nerves.

4. Herpes zoster of the occipital region with facial paralysis, hyperacousis and tinnitus.

5. Herpes zoster of the occipital region with involvement of facial and acoustic nerves.

6. Herpes zoster affecting the ear or adjacent region of the head with disturbance of the acoustic nerve but no facial paresis.

The sixth nerve is rarely involved in association with herpes of the ear region. In a few cases, the facial or the acoustic nerve was affected when the herpes occurred elsewhere on the body.

The general health may be affected in all cases of this type. Leucocytosis has also been described and occasionally an increase in both cells and protein content of the cerebrospinal fluid. The herpetic eruption is found in the area supplied by the fifth nerve in about 35 per cent. of the cases; in others it occurs in the areas of the seventh, ninth or tenth nerves. Sometimes it may arise simultaneously in the areas supplied by several nerves.

The author of this communication considers that the lesions of the facial and acoustic nerves are the result of herpetic infection of their ganglia. Occasionally herpetic infection of these nerves may occur without any eruption. Such cases have been recorded by Frankl-Hochwart under the heading of ' Polyneuritis cerebralis meniereformis.'

It is noteworthy that the author recommends that a herpetic eruption of the tympanic membrane should not be interfered with provided there is not much pain, as the opening of the middle ear may give rise to a secondary infection.

M.

[22] **The present conceptions of herpes** (Les conceptions actuelles de l'herpes).—M. Albeauz-Fernet and P. Collart. *Gaz. des hôp.*, 1933, **106**, 1467.

In 1904 Ravaut and Danet by means of lumbar puncture showed the constancy of nervous involvement in genital herpes and especially in recurrent herpes. From 1910 onwards the disease was considered an inoculable infectious disease. It is now generally admitted that herpes is a specific disease of which the cutaneous lesions represent only one manifestation. Multiple causes favour the appearance of the eruption, the most frequent being certain infectious diseases, cerebrospinal meningitis, pneumonia, spirochætosis icterohæmorrhagica, local infections, intoxications, endocrine disturbances, etc. These, however, are only occasional causes which, by the disturbances they bring about, provoke the hitherto latent virus. Recent work has shown that an invisible and filtrable virus is concerned. Levaditi considers it is an ultrafiltrant virus. The authors of this paper give in detail

the results obtained in the course of their experiences and describe the pathological anatomy and the clinical aspects of the affection which vary considerably according to the localization. As regards diagnosis, they stress the difficulty when the herpes lies at the level of the genital organs and particularly the confusion which may arise between herpes with confluent vesicles and a syphilitic chancre. Finally, they note that a meningitis may occur although the proof of its existence as a clinical entity is difficult to establish, the cerebrospinal fluid changes being very transient. According to Sendrail, a positive inoculation of the cerebrospinal fluid in the cornea of a rabbit would be of no definite value; it would confirm the presence of the virus in the organism but not its pathogenic rôle. An important bibliography is appended.

C. W. D.

[23] **Myotonia atrophica with cataract.**—Leo L. Mayer and Joseph A. Luham. *Arch. Neurol. and Psychiat.*, 1933, **30**, 810.

The authors review the literature and submit a report of three additional cases The principal features of the disease can be summarized as follows:—

Myotonia atrophica (myotonic dystrophy) is a distinct nosological entity characterized by: (1) myotonia, in the active form usually limited to the hand grasps; (2) muscular atrophy of a selective distribution; and (3) dystrophic extramuscular phenomena, chief among which is a distinctive form of presenile cataract. The disease is probably heredofamilial, as the studies of Fleischer indicate. It usually begins between the ages of 18 and 35 and predominantly affects males.

Active myotonia is ordinarily limited to the fist-closing muscles, but sometimes involves the tongue and other groups of muscles. Mechanical myotonia, shown by a persistent dimple or furrow at the point of impact when a muscle is percussed, is most commonly found in the thenar and hypothenar muscles and in the deltoids. The myotonic electrical reactions are often influenced by the presence of atrophy in the muscles examined. All three forms of myotonia are not usually found in the same muscle. Myotonia tends to appear early, before the development of atrophy, and may disappear with the advance of the atrophy.

The muscular atrophy is selective, involving the facial muscles, the sternocleidomastoids, the muscles of the forearms, the vasti of the thighs and the dorsiflexors of the feet. The hatchet-like physiognomy, combined with ribbon-like sternocleidomastoids and wasting of the muscles of the forearms, gives rise to a strikingly characteristic picture.

The extramuscular symptoms include cataract—essentially a presenile cataract—revealed on gross examination in about one-half of the published cases. However, cataract will probably be found to be one of the most nearly constant findings in this condition if the lenses are examined by means

XUM

of a slit lamp. Early, the appearance of fine, dust-like opacities under the anterior and posterior capsules is characteristic of this form of cataract; later, starlike formations may be found. Cataract is of great significance in the hereditary transmission of the disease, since members of affected families may present cataract alone (without muscular symptoms).

Testicular atrophy, monotonous nasal speech, acrocyanosis, premature baldness, increased secretion of tears and loss of tendon reflexes even in healthy-appearing muscles are dystrophic phenomena that are encountered with varying frequency in myotonia atrophica.

The pathological basis for the atrophy appears to have been found within the muscles themselves (rather than in their related motor cells within the spinal cord). There is some histological evidence to suggest that the vegetative nervous system within the central neuraxis may be pathologically implicated as the cause of the myotonia. The occurrence of cataract and of tetanic muscular phenomena in states of parathyroid deficiency has led investigators to search for evidences of parathyroid insufficiency in myotonia atrophica. In this regard, certain recent observers have stressed a diminished calcium content of the blood, signs of latent tetany and the cataract itself as indicating that parathyroid insufficiency is involved in the pathogenesis of myotonia atrophica.

R. M. S.

[24] **Posttraumatic paresis of the posterior cord of the brachial plexus** (Posttraumatische Paresen im Bereich des hinteren Bündels des Plexus brachialis).—J. HEMPEL. *Münch. med. Woch.*, 1934, **81**, 93.

THREE cases are recorded in which four to six months after a comparatively slight trauma of the shoulder region there was found weakness in the external rotation of the arm at the shoulder and in raising the arm forwards. The muscles over the scapula were wasted; in one case there was also slight wasting of the deltoid and in another winging of the scapula. In two of the cases cutaneous sensation was normal and the third showed diminished sensibility over the lower part of the scapula. In all three cases the electrical reactions were impaired in the supraspinatus and infraspinatus muscles. The electrical change found in the supraspinatus is remarkable as the trapezius was not apparently affected. The above symptoms are described as a consequence of a lesion of the suprascapular nerve which usually arises as a special branch from the outer cord of the brachial plexus, but in some individuals this nerve arises from the circumflex. The suprascapular nerve also supplies the teres minor and the upper part of the serratus magnus; consequently in some cases external rotation of the arm may be seriously impaired and there may also be some dislocation of the inner border of the scapula.

M.

PROGNOSIS AND TREATMENT

[25] **The treatment of juvenile general paralysis.**—Howard W. Potter. *Psychiatric Quarterly*, 1933, **7**, 593.

Of 60 cases of juvenile general paralysis 38 were treated with malaria or tryparsamide or both, 20 with common arsenicals and bismuth or mercury, and two with radiothermy and diathermy respectively. Of the 20 treated with common arsenicals, 17 continued to undergo a mental and physical deterioration and several of these died. In 27 of the 38 cases treated with malaria or tryparsamide the treatment was effective in so far as it prevented further deterioration; five of these gained a complete remission and nine a partial remission. In the great majority of instances a period of from two to five years had elapsed after the beginning of the treatment. In studying the factors that affect the prognosis in the 38 cases treated with malaria or tryparsamide the prognosis was found to be better in (*a*) patients who prior to the onset of the paresis were of normal mental level; (*b*) patients who were in or past adolescence when the symptoms developed; (*c*) those showing the expansive and confused reaction types; (*d*) those in whom the elapsed time between the onset of the disease and the treatment did not exceed two years. Sex, character of the onset and antiluetic treatment prior to onset did not appear to affect the prognosis favourably or unfavourably.

C. S. R.

[26] **Treatment of dementia paralytica with typhoid H. antigen vaccine.**—M. T. Schnitker. *Arch. Neurol. and Psychiat.*, 1934, **31**, 579.

Twenty-five patients with dementia paralytica, physically unsuitable for treatment with malaria, whole typhoid vaccine or diathermy, were treated with typhoid H antigen (flagellar) vaccine alone and in combination with tryparsamide.

In the author's opinion the symptomatic and serological improvement obtained by this method compares favourably with results obtained with other forms of fever therapy.

Typhoid H antigen vaccine is indicated for persons who cannot withstand the rigors of the other heroic forms of therapy because (*a*) although the hyperpyrexia equals that obtained with whole typhoid vaccine, the concomitant illness is far less severe; (*b*) it does not involve superimposing a second (and perhaps lethal) infection on an already existing one, as with malaria; (*c*) it does not involve the risk of burns and renal damage, as with diathermy; (*d*) its contraindications are but four, namely, (1) severe cardiorenal disease, (2) active pulmonary disease, (3) severe cachexia, and

(4) acute infection with a rapid sedimentation rate; (*e*) its administration and control are simple, and its use in the hands of the general practitioner, both in the hospital and in the home, is safe; (*f*) in Schnitker's hands it has not been associated with complications or sequelæ.

Improvement was found not to be directly proportional to the height of the temperature obtained, but seemed to be related to the total number of hours of fever. Better clinical results were obtained by combining the administration of tryparsamide with the fever treatment, the injections being given at the height of the fever.

R. M. S.

[27] **Studies in endocrine therapy in epilepsy.**—CALVERT STEIN. *Amer. Jour. Psychiat.*, 1934, **13**, 739.

THE results of therapy with a selected group of endocrine preparations on 68 epileptics, one narcoleptic, and 75 non-epileptic controls of both sexes are given. None of the preparations that were used was specific for convulsions—neither curing them in the epileptics, nor causing them in the controls. There was some evidence, however, that in a few cases overstimulation of the ovaries might be indirectly provocative of convulsions. The majority of those that received thyroid substance, either alone or in combination with other glands, showed definite clinical improvement in metabolism, bowel activity, and general wellbeing. Blood-pressures tended to be subnormal and there was some evidence that dried suprarenal gland by mouth, as well as thyroid, will raise the pressure from 10 to 30 mm. and maintain the rise as long as medication is continued. The best results in both epileptics and controls were obtained with pituitary, thyroid and suprarenal, and pluriglandular therapy was more efficacious than single therapy except in treatment with thyroid. Endocrine therapy should be but one part of a general therapeutic programme, for there is no known endocrine disorder that appears to be specifically responsible for the production of epileptic seizures. Patients with obesity and constipation offer the best prospects for improvement with oral administration of thyroid and whole pituitary in combination. Those who improved in general health while under treatment did not show any reduction in the frequency or severity of their fits, but did show a lessening of postconvulsive debility, headache and weakness, and also a marked shortening of the post-convulsive period of convalescence. It is reasonable to expect that if the clinical improvement in metabolism, gastrointestinal function, and general wellbeing of epileptics can be maintained for a period of several years at least, the convulsive threshold may also rise to the point of overcoming their seizures.

C. S. R.

Psychopathology

PSYCHOLOGY

[28] **A statistical study of dreams in relation to emotional instability.**—F. K. Berrien. *Jour. Abn. Soc. Psychol.*, 1933, **28**, 194.

Students taking introductory courses in psychology were experimentally investigated in order to throw light on the question—Do emotionally unstable individuals recall more dreams than their relatively stable associates? It was concluded that something besides emotional instability was operative in determining the frequency of dreams. The evidence here set forth gives no foundation for the Freudian concept of dreams and must be looked upon as putting the analysts on the defensive when they begin talking about the relationship between dreams and emotional instability. On the contrary, no evidence appears here to question the assumption of H. J. Watt, who says the chief difference between the thinking of daily life and of dreams must surely lie in the initial source of each. In sleep we start usually, or after the slightest reflection from within or without the body, with favoured but unsatisfied or unrealized attitudes of mental action. These are the parts of our mind that have the most latent energy and are least asleep.

C. S. R.

NEUROSES AND PSYCHONEUROSES

[29] **Psychoneuroses of childhood: their ætiology and treatment.**—Melitta Schlideberg. *Brit. Jour. Med. Psychol.*, 1933, **13**, 313.

The neurotic symptoms of childhood are by no means due solely to wrong behaviour on the part of the parents; they occur also under excellent environmental conditions. They are caused by conflicts which are at work in every child. These can be increased or diminished through environmental influence but can in no case be avoided completely. Such symptoms sometimes appear in the first weeks of life. Some infants from the very beginning show anxiety and sometimes as early as the second or third month of life this anxiety takes on the form of a definite phobia. There are others who from the earliest age suffer from conversion symptoms, vomiting, constipation, or fits. Many children develop anxiety in the second or third year, often of psychotic character. 'Naughtiness,' lying and stealing as well are mostly related to neurotic conflicts. Asocial behaviour and abnormal character development often start in early childhood. Frequently enough such symptoms disappear in later life, but this often merely indicates that the conflict is finding no outlet—a psychic situation which may be unfavourable for the child's development. Disappearance or diminution of neurotic symptoms in the latency period is caused by strengthening of the ego and

weakening of instinctual urges. The child attempts to suppress or conceal its conflicts, forbidden instinctual desires and troublesome neurotic symptoms, and in doing so is often strongly influenced by its environment. Mental balance acquired in the latency period through suppression of instinctual energies is upset by the surge of reinforced instinct at puberty. Outbreaks of psychosis or neurosis often occur at puberty and abnormal character development is usually recognized at this age.

C. S. R.

PSYCHOSES

[30] **Clinical variables in schizoid personalities.**—Jacob Kasanin and Zitha A. Rosen. *Arch. Neurol. and Psychiat.*, 1933, **30**, 538.

The aim of this study was to answer two questions: (*a*) Do patients with similar schizoid personalities have similar clinical pictures when they break down? (*b*) Can the schizoid personality be described in terms of a given constellation of traits? This type of personality is defined as possessing the following five characteristics: few friends, shyness, seclusiveness, closed-mouthedness, and extreme sensitivity. Only 33 of 327 patients were found to have this combination of traits in prepsychotic life; 24 of these had schizophrenia out of a total of 151 with schizophrenia. The clinical pictures in these cases varied greatly from case to case with only slight superficial resemblances. In spite of the alleged unfavourable constellation of traits in the personality, the recovery rate was higher than in an unselected group of schizophrenic patients or in general hospital populations. Analysis of factors favouring recovery did not reveal any single especially significant condition in all cases. It seems that certain conditions in present-day culture lead to the hospitalization of maladjusted males at an earlier age than females. Only 15.9 per cent. had the specific combination of traits delineating the schizoid personality. Significantly associated with the nucleus of five traits were 'little self-assertiveness,' 'no sense of humour,' 'frequent day-dreaming,' 'little output of energy,' 'feeling of inferiority,' 'fusses over pain,' 'very absent-minded,' 'neurotic traits in childhood,' and 'unusual attachments' to some member of the family in adult life. In the transition from childhood to adult life, the neurotic traits decreased while all the schizoid traits increased. A review of various clinical data reveals that the most frequent factors associated with the schizoid personality were an over-attachment to the family, maternal over-protection, paternal neglect, physical defects and anomalies present in practically all of the cases, and unsatisfactory heterosexual adjustments. The description of the schizoid personality by traits does not give a true picture of the personality or of its dynamic relation to the psychosis.

C. S. R.

[31] **The experiential aspects of dementia præcox.**—ANTON T. BOISEN. *Amer. Jour. Psychiat.*, 1933, **13**, 543.

THIS study proceeds from the hypothesis that dementia præcox has to do with the urge for self-realization and that it consists of two chief types. One has malignant tendencies. Here the urge for self-realization has either become short-circuited as a result of the closing of the configurations on a level which leaves the individual isolated from his fellows and shut off from his own objectives. In the other there is generally the awareness of personal failure and inability to face the inner bar of judgment. Thus the terrified individual becomes preoccupied with a narrow circle of ideas and passes into an abnormal condition. Though an illustrative case is given to serve as a base-line for an examination of the inner meaning of the schizophrenic experience, the findings here are founded upon a study of 176 cases. In general these were found to have more than their share of hereditary taint; more than their share of unfavourable environmental influences; and while seldom feebleminded they were somewhat below par intellectually. Physically they were a trifle undersized and had less drive and vigour than normal. Somewhat more subject to physical disease, about two-thirds had more or less endocrine malfunction. But in all this there was nothing distinctive. In 36 per cent. there were clear maladjustments in the fields of sex, vocation, and society, and in 75 per cent. the same could be said of two of the fields.

Following the idea that the primary evil in dementia præcox involves the sense of personal failure, isolation and an intolerable loss of self-respect result. Three methods of dealing with this sense of personal failure were traced —*drifting* into mental refuges, the dream world becomes the real world. Through refusing to admit error or defeat, others resort to *delusional misinterpretation*. Few escape becoming aware of their danger with more or less emotional disturbance, and in extreme forms *panic* may ensue. These general reaction types usually occur in combinations.

In 55 of the cases the onset was sudden and involved acute emotional disturbance; in 69 it was of the subacute type; and in 52 it was insidious. Only in seven cases were there any factors in the immediate life situation which might account for the mental disturbance. The sense of failure may be recognized, concealed, or evaded. Out of the 176 cases, 130 showed manifestations of concealment. This is found in four chief forms, the most frequent being the *externalisation of conscience* (113 cases), as seen in accusing voices, the mind being read, ideas of being poisoned or killed. *Transfer of blame* as noted in paranoid ideas of electrical currents, or being superpersonally influenced was evident in 70 cases. *Fictitious self-importance* appeared in a large number, and in 10 was sufficiently powerful to effect a comfortable delusional reconstruction. Lastly, the *incapacitation* reaction in which physical illness is made to bear the responsibility for the personal

XUM

failure was noted in 29 cases. The chances of recovery depend largely on the possibility of making an adjustment in the life situation which will be acceptable to the patient. Where the situation is lacking in constructive factors and admits of no solution, the patient may be restored temporarily but is not likely to remain well. The significance of the reaction patterns must be carefully considered, and the malignant tendencies must be distinguished from the acute disturbance characterized by ideas of death, of cosmic catastrophe and cosmic identification. The more sudden the onset and the more acute the disturbance, the more likely is the patient to recover. Suffering may be looked upon as remedial. The presence of inappropriate moods and attitudes is a bad sign. Attitudes of frankness and self-blame are favourable indications. 'Voices' indicate a stirring of the deeper mental levels, something which in itself may be helpful as well as destructive. Their chief significance lies in what they reveal as to the inner trends and attitudes.

C. S. R.

[32] **Order of birth in manic-depressive reaction.**—HAROLD H. BERMAN. *Psychiatric Quarterly*, 1933, **7**, 430.

OUT of 100 cases of manic-depressive psychoses 48 were found to be among the first-born. Twenty-two cases were among the last born. The reaction to the birth of a younger member in a family frequently appeared to be a predisposing factor. Early childhood disorders should be treated as manic-depressive reactions in the hope of averting frank attacks of psychosis in later life.

C. S. R.

[33] **The blood cholesterol in schizophrenia.**—JOSEPH M. LOONEY and HAZEL M. CHILDS. *Arch. Neurol. and Psychiat.*, 1933, **30**, 567.

APPROXIMATELY 50 men with schizophrenia were studied at intervals for seven months. The cholesterol content was determined by the method of Myers and Wardell. The mean values were: 146 ± 3 mg. per 100 c.c. for the first period, 161 ± 2.8 mg. for the second period, and 166 ± 2.5 mg. for the third period. The mean value for 26 normal men was 175 ± 5.2 mg. Both the schizophrenic patients and the controls showed great variation in the cholesterol values, the former having a standard deviation of about 20 mg., and the latter of 27 mg. The difference between the mean value for the first period and those for the last two periods is believed to be due to a seasonal valuation in the cholesterol content of the blood. No correlations could be shown between the blood cholesterol and the basal metabolic rate or the emotional status. Schizophrenia seems to be characterized by a slight degree of depression of the cholesterol content of the blood.

C. S. R.

[34] **The fæcal flora in catatonic dementia præcox.**—Barbara McGinn, Mary E. Raney, and Nicholas Kopeloff. *Psychiatric Quarterly*, 1933, **7**, 260.

Bacteriological examination of the fæcal flora of four catatonic dementia præcox patients was repeated monthly for four months. The hydrogen ion concentration, total bacterial count, predominant aerobes and anaerobes, all fell within the limits of variation with the normal. The incidence of *B. acidophilus* was less than normal, but the character of the flora was fermentative rather than putrefactive. No unusual microbe was isolated with sufficient consistency to indicate that the bacterial flora might be causally related to the mental disease process.

C. S. R.

PSYCHOPATHOLOGY

[35] **An analytical review of a series of cases of insanity with pregnancy.**—C. B. Bamford. *Jour. of Ment. Sci.*, 1934, **80**, 58.

In this review the old conception that these cases offer a favourable prognosis from the point of view of complete recovery of the mother is by no means confirmed. At Rainhill Hospital insanity with pregnancy (taking no account of puerperal and lactational cases) was found to be comparatively rare, accounting for less than 10 per cent. of total admissions. Ninety-seven cases are here examined. In only 17 cases was there evidence of any psychopathic inheritance, and of these only six recovered. In over 25 per cent. it seemed that some associated disease brought an extra strain to bear and was responsible for the breakdown. Over 75 per cent. were admitted beyond the seventh month, and it would appear that the second half of pregnancy is the time fraught with risks of serious mental disturbance, particularly the seventh or eighth month. The absence of obstetrical difficulties and complications seems worthy of mention. The puerperium, too, was especially free from infective processes. The conclusion was arrived at that a large number of cases were potential psychopaths and would have become insane sooner or later quite independent of pregnancy. Amongst the unrecovered cases (59) there were 12 mental defective, 13 epileptics, seven general paralytics, 12 with dementia præcox, 11 with manic-depressive insanity, two with delusional psychoses, and two with alcoholic dementia. The problem of the correct diagnosis of the cases that recovered exercised the mind of the writer for some time. Most were regarded as confusional (for want of a better title) or manic-depressive and a few had mixed symptoms which did not fit suitably into either category. Nevertheless, the confusional cases did not conform to the usual type. There was scarcely any associated bodily disturbance of any severity and very little reliable evidence of any severe degree of bodily intoxication. With the exception of three cases which improved before

XUM

delivery most failed to show any improvement until the second month. For a time after delivery there was an acute exacerbation of the mental symptoms. In six of the cases improvement was deferred until six months had passed, but they then made a full recovery. In the average case, recovery may reasonably be expected about the third month following confinement, and this would make the probable duration of such a psychosis as six months. It is to be noted that in no case was premature labour artificially brought about, and it is thought that there must be very few cases of insanity which either in the maternal or fœtal interest require such a step.

C. S. R.

[36] **The nature of emotion and its relation to antisocial behaviour.**—FRED BROWN. *Jour. Abn. Soc. Psychol.*, 1934, **28**, 446.

FROM this study it is concluded that the ' psychopathic personality ' is not to be attributed to an organic or functional defect. Psychopathic behaviour or emotional maladjustment is strongly indicative of trial-and-error attempts to utilize the constantly accumulating energy generated in the presence of a stress-strain situation for which the individual possesses no adequate outlet. Consequently, otherwise normal reactions become overcharged with energy and result in antisocial modes of response or else less adequate responses are utilized to relieve the tension state. The fault lies in the *type of behaviour* utilized rather than in any fundamental physio-organic disorder. Since all social behaviour is learned, there is great hope for the ultimate elimination and prevention of antisocial modes of conduct now designated as ' emotional ' in nature.

C. S. R.

[37] **Some observations on lipoid metabolism in mental disorders.**—J. S. SHARPE. *Jour. of Ment. Sci.*, 1934, **80**, 75.

THE result of these investigations shows that the lecithin content of the blood in mental disorder exhibits no important variation from normal. The cholesterol content of the blood in early dementia præcox is decreased by about 25 per cent. Later there is an increase by about 30 per cent., as chronicity advances, and it remains at that figure. This may be due to a hyperactivity of the suprarenal glands. The coefficient of utilization is low. In melancholia and confusional insanity the blood cholesterol is slightly on the high side, but the variations are small. The coefficient of utilization is very low in these groups, denoting deficient oxidation and low metabolic activity. Recurrent mania cases show a very high blood cholesterol, particularly during an acute attack. This cyclic nature of the condition seems to suggest some derangement in metabolic activity, probably centred round the suprarenal glands, as evidenced by the blood cholesterol increase. Further, the coeffi-

cient of utilization is very high, indicating increased metabolic rate. There exists in the blood in certain melancholic and confusional states a powerful depressor substance having a choline-like action on the isolated frog heart. This substance is antagonized by adrenaline. Normally, the depressor substance is in such small concentration as to be almost undetectable. In dementia præcox and recurrent mania this substance exists in very small quantities, approaching the normal figure as determined by the physiological test. Evidence points to a deficiency or absence of choline in melancholia and confusional insanity. This substance may be conveniently termed 'cholinase.' The clinical feature of these cases is that of hypotonia.

C. S. R.

[38] **Studies of blood-sugar curves in mental disorders.**—S. KATZENELBOGEN and E. FRIEDMAN-BUCHMAN. *Amer. Jour. Psychiat.*, 1933, **13**, 321.

THE carbohydrate metabolism, as tested by the blood-sugar curves, was studied in 116 psychotic patients. These included 31 cases of psychoneurosis, 50 cases of manic-depressive insanity (out of which six were manic), 20 of schizophrenia, and seven cases of organic psychosis. The curves were evaluated, first, by the intensity of the alimentary hyperglycæmia (following the ingestion of 50 gm. of glucose); second, by the extension of the glycæmic reaction over a two-hour period (hyperglycæmic index); and third, by both the height and extension of the curve combined (hyperglycæmic area). Abnormal curves were obtained in each psychotic group; in the psychoneuroses, 64 per cent.; in mild manic-depressives, 72.9 per cent.; in the schizophrenics 60.7 per cent., when the curves were evaluated by the climax of the hyperglycæmia. When estimated by the hyperglycæmic area, the values were 62.5, 79.2, and 72.7 per cent. respectively; in the organic psychoses, 100 per cent., judged by both methods of evaluation. The abnormal curves showed similar characteristics in the four reaction types. It is believed that the apparently similar disturbance of the carbohydrate metabolism in the different psychotic reaction types may be related to a common denominator, that is, affective disorder. Thus, the abnormal blood-sugar curves in these patients were considered as physiological accompaniments of psychobiological reactions.

C. S. R.

[39] **Blood and urine chemistry during the specific dynamic action of glycine in normal subjects and in schizophrenics.**—CHARLES REID. *Jour. of Ment. Sci.*, 1934, **80**, 379.

AFTER glycine the amino-N content of the blood reached its maximum near the end of the second hour. Blood urea-N increased slowly and steadily

XUM

during the period of observation. The mean increase in the seventh hour after glycine was about 4·0 mgm./100 c.c., but the actual increase in a particular case appeared to depend entirely on diuresis and the urea excreted. Blood-sugar decreased about 10-15 mgm. per 100 c.c. after glycine ingestion, but tended to approach the fasting level in the course of six to seven hours. The non-glucose-reducing substances were not significantly altered. The non-protein nitrogen fraction (non-urea and amino-N) of the blood was increased after glycine administration. Nitrogen elimination was much increased also and the excess urea-N excretion during six hours of the post-glycine period amounted to 0·23 of the nitrogen given as glycine. The total nitrogen of the urine (less the amino- and urea-N fractions) was increased after glycine, and this was due either to increased elimination or to increased production in the tissues, or to both. Sulphate excretion was maintained at a higher level than was found for controls during the postabsorptive period. It appeared that the sulphate excretion provided a more reliable index of specific dynamic action than the nitrogen excretion during the period of observation in the experiments dealt with here. The examination of schizophrenics after glycine ingestion did not reveal any striking deviation as to their blood and urine chemistry from those in normal subjects. The character of the mean blood amino-N and urine amino-N curves suggested delay in the absorption of the ingested material as compared with normal. Blood nitrogen and urine nitrogen estimations were not significantly different in schizophrenics from the normals. Approximately the excess urea-N excretion after glycine amounted to 0·21 of the nitrogen ingested as glycine. Sulphate excretion on the whole was less for schizophrenics than for the normals, and this could be due to decreased specific dynamic action in these psychotics or to a diminished absorption rate of the ingested material. Blood urea values in schizophrenics and in normal controls after the giving of 15 gm. urea in 100 c.c. were suggestive of delayed absorption, since the rise in blood urea was slower in the former. Conclusions based on blood urea values after glycine without consideration of the urea excretion are not justifiable. The attempt to demonstrate variations in the specific dynamic action of foodstuffs or glycine by ingestion methods in psychotics is also unjustifiable, in view of the variations in the processes of absorption which have been demonstrated in both normal and psychotic subjects.

C. S. R.

PROGNOSIS AND TREATMENT

[40] **Prognosis in manic-depressive psychoses.**—Reginald R. Steen. *Psychiatric Quarterly*, 1933, **7**, 419.

From a study of 493 cases it is concluded that an individual would be most likely to recover from his manic-depressive attack if he had a normal previous

personality, a clear heredity, no previous attacks, or a previous attack between his 20th and 30th birthdays, and an abrupt onset of a typical manic or depressive reaction with no delusions or hallucinations. The average duration of the writer's recoveries was 1·51 years.

C. S. R.

[41] **The treatment of narcissistic neuroses and psychoses.**—L. Pierce Clark. *Psychoanalytic Review*, 1933, **20**, 304.

While we may learn a great deal about narcissism by applying the technique of ordinary analysis, we fail to help the narcissist. Some new method must be evolved. The attitude toward the mental disease is one of 'watchful waiting,' and yet a fairly large number of cases, for all practical purposes, recover. In each individual case it seems as though some combination of fortuitous circumstances has had influence. The inference is that the therapy of 'watchful waiting' allows the ego to take its own time in gradually adapting itself to the outer world. The value of the fortuitous circumstances mentioned apparently consists in their providing to the weak ego the love and support it requires, and in their granting it the extended opportunity for slowly making ready for the changes which the instincts and reality impose. The purpose of a psychoanalytic technique would be to make such an outcome less the result of chance, more the product of enlightened effort. It may be that the relationship of analyst and patient will never assume the conditions of an ordinary transference-analysis; but through a modified technique the ego is given the chance to resume its interrupted growth at a speed of its own choosing. It can be made possible to discharge emotions without at once facing the retributions of the real world. It should be a relationship where the analyst goes with the patient rather than the reverse. Thus is promised the possibility of overcoming that primary mountain of resistance which has hitherto defeated most attempts to analyse the narcissist.

The early stages of treatment may conform largely with the pleasure-principle, but eventually as the transference becomes stronger there must be slowly offered an influence towards accepting the reality-principle. The ultimate aim of therapy would be to bring together narcissistic libido and object-libido into a united release upon real activities. It must be held that it is possible to strengthen the ego. All that is asked of the patient is that he talk about himself. The problem becomes one of allowing the analyst to be recognized as not completely attached to the patient's ego but requiring some projection of libido in order to gain narcissistic satisfactions. Once a narcissistic transference is established the procedure is very similar to that followed in the analysis of the transference neuroses. The danger may be that too much may be expected of the narcissistic patient.

C. S. R.

XUM

[42] **The treatment of dementia præcox by continuous oxygen administration in chambers and oxygen and carbon dioxide inhalations.**—L. E. Hinsie, A. L. Barach, M. M. Harris, E. Brand and R. A. McFarland. *Psychiatric Quarterly*, **1934, 8, 34.**

Five patients resided continuously for two and a half months in an oxygen chamber at a concentration of approximately 50 per cent. oxygen. During this time they received treatments of carbon dioxide and oxygen daily. After each carbon dioxide inhalation attempts were made to establish communicability with the patients. Two of the five gained a state of remission and the clinical history of these had indicated a favourable prognosis. A second group of five patients were treated similarly except that no communicability attempts were made. None of these showed improvement. A third group of five resided in the oxygen dormitory without carbon dioxide treatment and without communicability attempts. None of these showed any improvement. A fourth group of five, living under normal atmospheric conditions, were given daily inhalations of carbon dioxide and oxygen. Here one showed clinical improvement but did not gain a remission.

The blood chemical studies showed no effect of long-continued oxygen inhalation on the urea nitrogen, uric acid or blood sugar content of venous blood. Basal metabolic determinations varied so much that no consistent conclusions could be drawn. Under various psychological tests no consistent improvement was observed in the patients who did not gain a remission. From observations made, it does not appear that oxygen and carbon dioxide treatment of catatonic dementia præcox patients is to be advocated as a general therapeutic procedure.

C. S. R.

Reviews and Notices of Books

The Human Personality. By Louis Berg, M.D. London: Williams and Norgate. 1933. Pp. 309. Price 8s. 6d.

An ambitious attempt is made in this book, written from the sociologist's point of view, to sum up our knowledge of human personality. The author reviews the conclusions, as he interprets them, reached by biology, genetics, endocrinology, psychology, criminology and psychiatry regarding the nature of man and the determinants of his conduct.

The result is disappointing. Statements which cannot be supported are numerous. The section upon 'The Glandular Basis of the Personality' has many such. For example, we are told (p. 67) that the personality may be controlled by overaction of the posterior pituitary. No evidence is given, or available, to prove this. Dr. Berg describes a type of personality as the 'status thymico-lymphaticus' and tells us how it may be 'cured.' In 1931 the Status Lymphaticus Committee declared that there was no evidence that so-called 'status thymico-lymphaticus' had any existence as a pathological entity. Many old errors are repeated and no new information given in the chapter on 'Personalities in Conflict.' Statistics contradict the author's statement that 'hysteria is the most common of all neuroses.' Few will agree that 'Charcot was the first to use hypnotism scientifically'—or, perhaps, that he ever used it scientifically.

The book was written 'in view of the acute need of well integrated studies of our sometimes bewilderingly complex life.' It fails to satisfy this 'acute need,' and we must still await 'a synthesis of modern research.'

Psychology and Psychotherapy. By William Brown, D.M., D.Sc., F.R.C.P., Wilde Reader in Mental Philosophy in the University of Oxford, etc. London: Edward Arnold. 1934. Pp. 252. Price 12s. 6d.

The previous editions of this work (first published in 1921) have been reviewed in this Journal. The third edition has been enriched by the author's wider experience; and in aim and plan it is virtually a new book. Dr. Brown, while accepting much of the systems of Freud, Jung and others, declines the label 'eclectic,' preferring to regard his position in and contribution to psychology and psychotherapy as 'synthetic.' The term is not a happy one—it suggests an artificial product. This is, however, far from being the

case. The views here expounded have stood the test of time and practical application.

The book gives a balanced survey of medical psychology and as such it can be unreservedly commended. The appendices, five in number, occupy about a fifth of the book; they will appeal chiefly to the trained psychopathologist. An excellent index is provided.

E. A. B.

95

BRITISH MEDICAL ASSOCIATION

IMPORTANT NOTICE

SEE OVER—

96

BRITISH MEDICAL ASSOCIATION

ANNUAL MEETING, MELBOURNE, SEPTEMBER, 1935.

The 103rd Annual Meeting of the British Medical Association will be held in Melbourne in the week commencing Monday, September 9th, 1935. Included among the Scientific Sections at that Meeting will be one on Neurology and Psychological Medicine, and as many interested in this subject will doubtless be going to Australia, it would facilitate the arrangements if the Medical Secretary of the Association could be informed of their intentions at the earliest possible moment.

The journey to Melbourne and back will be by means of a most attractive "Round-the-World" Tour, which has been arranged at a very reasonable figure. Full particulars of the Tour can be had on application to the Financial Secretary of the Association at B.M.A. House, Tavistock Square, London, W.C.1, and many bookings have already been made through the official agents for the Council, Messrs. Pickford's Travel Service, 205/206 High Holborn, London, W.C.1.

XUM